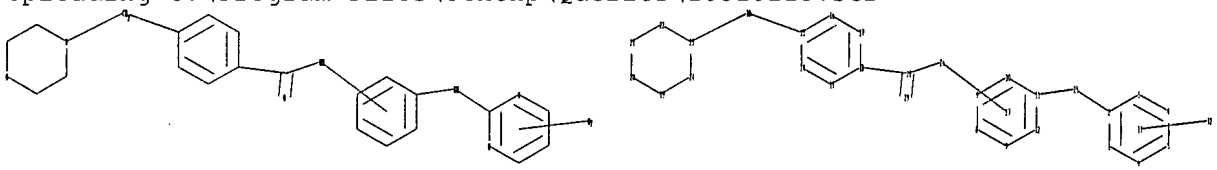
=>
Uploading C:\Program Files\Stnexp\Queries\10518213.str

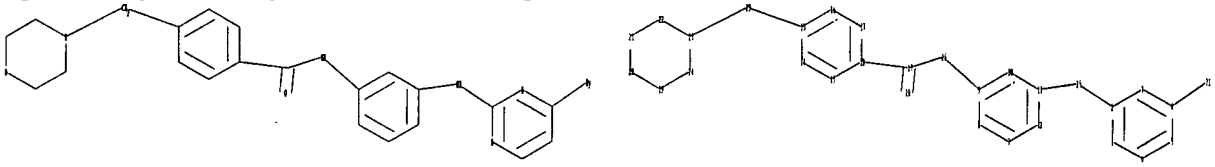


chain nodes :
25 26 28 29 30 32
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23
24
chain bonds :
2-25 11-25 15-30 18-28 23-30 26-28 28-29
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 13-14 13-18
14-15 15-16 16-17 17-18 19-20 19-24 20-21 21-22 22-23 23-24
exact/norm bonds :
2-25 11-25 19-20 19-24 20-21 21-22 22-23 23-24 26-28 28-29
exact bonds :
15-30 18-28 23-30
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 13-14 13-18
14-15 15-16 16-17 17-18
isolated ring systems :
containing 1 : 7 : 13 : 19 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom
20:Atom 21:Atom 22:Atom 23:Atom 24:Atom 25:CLASS 26:CLASS 27:Atom 28:CLASS
29:CLASS 30:CLASS 32:Atom 33:Atom
Generic attributes :
32:
Saturation : Unsaturated
Number of Carbon Atoms : less than 7
Number of Hetero Atoms : Exactly 1
Type of Ring System : Monocyclic

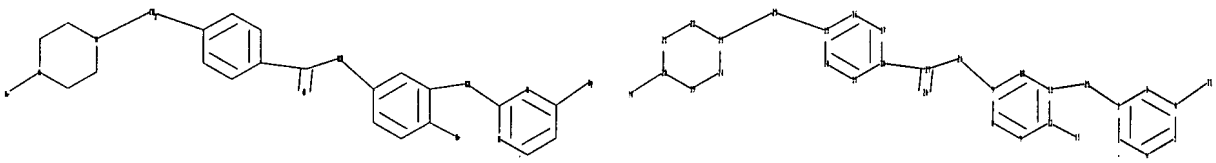
Element Count :
Node 32: Limited
C,C5
N,N1
O,O0
S,S0

```
L1      STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1              STR
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

Structure attributes must be viewed using STN Express query preparation.


=> s l1 sss sam
SAMPLE SEARCH INITIATED 17:05:51 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -       44 TO ITERATE

100.0% PROCESSED       44 ITERATIONS                                5 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          483 TO     1277
PROJECTED ANSWERS:               5 TO      234

L2            5 SEA SSS SAM L1

=> =>
Uploading C:\Program Files\Stnexp\Queries\10518213 (a).str
```



```
chain nodes :
25  26  27  28  29  31
ring nodes :
1  2  3  4  5  6  7  8  9  10  11  12  13  14  15  16  17  18  19  20  21  22  23
24
chain bonds :
2-25  4-31  9-26  11-25  15-29  18-27  23-29  26-27  27-28
ring bonds :
1-2  1-6  2-3  3-4  4-5  5-6  7-8  7-12  8-9  9-10  10-11  11-12  13-14  13-18
14-15  15-16  16-17  17-18  19-20  19-24  20-21  21-22  22-23  23-24
exact/norm bonds :
2-25  4-31  9-26  11-25  19-20  19-24  20-21  21-22  22-23  23-24  26-27  27-28
exact bonds :
15-29  18-27  23-29
normalized bonds :
1-2  1-6  2-3  3-4  4-5  5-6  7-8  7-12  8-9  9-10  10-11  11-12  13-14  13-18
14-15  15-16  16-17  17-18
isolated ring systems :
containing 1 : 7 : 13 : 19 :
```

```
Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
11:Atom  12:Atom  13:Atom  14:Atom  15:Atom  16:Atom  17:Atom  18:Atom  19:Atom
20:Atom  21:Atom  22:Atom  23:Atom  24:Atom  25:CLASS  26:CLASS  27:CLASS  28:CLASS
 29:CLASS  31:Atom
Generic attributes :
31:
Saturation             : Unsaturated
Number of Carbon Atoms : less than 7
Number of Hetero Atoms : Exactly 1
Type of Ring System    : Monocyclic

Element Count :
Node 31: Limited
    C,C5
    N,N1
    O,O0
    S,S0




L3      STRUCTURE UPLOADED

=> d l3
L3 HAS NO ANSWERS
L3              STR

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

Structure attributes must be viewed using STN Express query preparation.


=> s l3 sss sam
SAMPLE SEARCH INITIATED 17:08:22 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      174 TO ITERATE

100.0% PROCESSED      174 ITERATIONS                                5 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:         2689 TO     4271
PROJECTED ANSWERS:               5 TO      234

L4            5 SEA SSS SAM L3

=>
Uploading C:\Program Files\Stnexp\Queries\10518213 (b).str
```



chain nodes :
25 26 27 28 29 31 33 34
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23
24
chain bonds :
2-25 4-31 9-26 11-25 12-33 15-29 18-27 20-34 23-29 26-27 27-28
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 13-14 13-18
14-15 15-16 16-17 17-18 19-20 19-24 20-21 21-22 22-23 23-24
exact/norm bonds :
2-25 4-31 9-26 11-25 19-20 19-24 20-21 21-22 22-23 23-24 26-27 27-28
exact bonds :
12-33 15-29 18-27 20-34 23-29
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 13-14 13-18
14-15 15-16 16-17 17-18
isolated ring systems :
containing 1 : 7 : 13 : 19 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom
20:Atom 21:Atom 22:Atom 23:Atom 24:Atom 25:CLASS 26:CLASS 27:CLASS 28:CLASS
29:CLASS 31:Atom 33:CLASS 34:CLASS
Generic attributes :
31:
Saturation : Unsaturated
Number of Carbon Atoms : less than 7
Number of Hetero Atoms : Exactly 1
Type of Ring System : Monocyclic

Element Count :
Node 31: Limited
C,C5
N,N1
O,O0
S,S0

L5 STRUCTURE UPLOADED

```
=> d l5
L5 HAS NO ANSWERS
L5              STR

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

Structure attributes must be viewed using STN Express query preparation.


=> s l5 sss sam
SAMPLE SEARCH INITIATED 17:18:46 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      174 TO ITERATE

100.0% PROCESSED      174 ITERATIONS                                5 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:         2689 TO     4271
PROJECTED ANSWERS:               5 TO      234

L6            5 SEA SSS SAM L5

=> s l5 sss ful
FULL SEARCH INITIATED 17:18:53 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -     3892 TO ITERATE

100.0% PROCESSED     3892 ITERATIONS                              104 ANSWERS
SEARCH TIME: 00.00.01

L7           104 SEA SSS FUL L5

=> => s l7
L8         2911 L7

=> s mesyl?
L9        15495 MESYL?

=> s hydrat?
L10      237801 HYDRAT?

=> s l9 or l10
L11      253097 L9 OR L10

=> s l8 and l11
L12        1175 L8 AND L11

=> s l8 and l9
L13        1155 L8 AND L9

=> s l13 and l10
L14           6 L13 AND L10

=> d l14 1-6 bib,ab,hitstr
```

L14 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1337749 CAPLUS
DN 146:93522
TI Diagnostic and therapeutic methods for use of dasatinib in imatinib-resistant cancers and/or individuals with oncogenic c-kit gene mutations
IN Lee, Francis Y.; Heinrich, Michael C.
PA Bristol-Myers Squibb Company, USA; The United States of America as Represented by the Department of Veteran Affairs; Oregon Health and Science University
SO PCT Int. Appl., 115pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006135790	A1	20061221	WO 2006-US22564	20060609

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

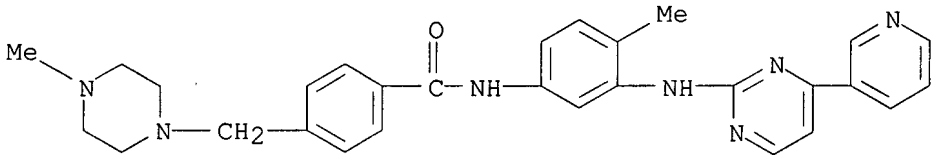
PRAI US 2005-689113P	P	20050609	
US 2005-736668P	P	20051115	
US 2005-748418P	P	20051208	

AB The invention relates to methods of identifying and treating individuals with protein tyrosine kinase associated disorders that have, or may, become resistant to treatment with a kinase inhibitor such as imatinib due to a gain-of- function mutation in c-kit tyrosine kinase. The invention claims methods, such as allele-specific PCR, for detection of gene c-kit mutations that result in substitutions of tyrosine, phenylalanine, valine, or histidine for the wild-type aspartic acid at residue 816 of the c-kit protein. Methods of treatment include administering dasatinib/BMS-354815 alone or in combination with another kinase inhibitor, specifically rapamycin. BMS-354815 inhibited ligand-dependent autophosphorylation of wild-type c-kit kinase and ligand-dependent cell proliferation in a human myeloid leukemia cell line. BMS-354815 also inhibited cell proliferation and induced apoptosis in c-kit V560G mutant cells and in a spontaneously occurring murine mastocytosis cell line which expresses a KIT D814Y mutation that is homologous to the human D816Y mutation. Imatinib inhibited the kinase activity of wild-type c-kit but showed minimal activity towards K816Y, D816F, or D816V mutant c-kit proteins. The c-kit mutations in codon 816 are in the activating loop region and gain-of-function point mutations have been reported in systemic mast cell disorders (D816Y, D816F), AML (D816Y), and seminomas (D816Y, D816H). Dasatinib/BMS-354825 blocked phosphorylation of MAPK1/2 and STAT3, which are c-kit dependent downstream signaling pathways. Combining dasatinib with rapamycin had an additive to synergistic anti-proliferative effect on cells expressing D816V c-kit protein.
IT 152459-95-5, Imatinib 220127-57-1, Imatinib mesylate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(diagnostic and therapeutic methods for use of dasatinib in imatinib-resistant cancers and/or individuals with oncogenic c-kit gene mutations)

RN 152459-95-5 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



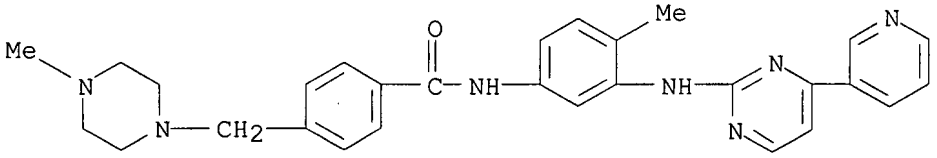
RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

CRN 152459-95-5

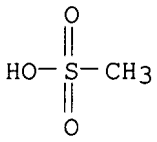
CMF C29 H31 N7 O



CM 2

CRN 75-75-2

CMF C H4 O3 S



RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

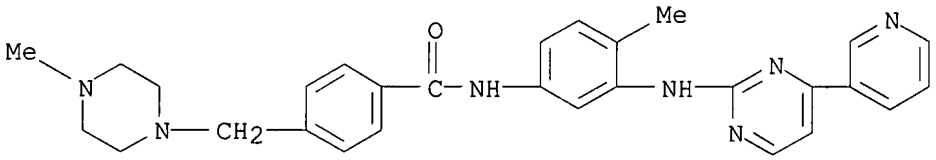
L14 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:1259339 CAPLUS
DN 144:17165
TI Method of using, and compositions comprising, immunomodulatory compounds for the treatment and management of myeloproliferative diseases
IN Zeldis, Jerome B.
PA Celgene Corporation, USA
SO PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005112928	A1	20051201	WO 2004-US14003	20040505
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004319816	A1	20051201	AU 2004-319816	20040505
CA 2565447	A1	20051201	CA 2004-2565447	20040505
EP 1746995	A1	20070131	EP 2004-751399	20040505
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, HR, LT, LV, MK				
CN 1984657	A	20070620	CN 2004-80043535	20040505
KR 2007019754	A	20070215	KR 2006-725518	20061204
PRAI WO 2004-US14003	A	20040505		

OS MARPAT 144:17165
AB Methods of treating, preventing, and/or managing a myeloproliferative disease are disclosed. Specific methods encompass the administration of an immunomodulatory compound, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof, alone or in combination with a second active agent, and/or the transplantation of blood or cells. Particular second active agents are capable of suppressing the overprodn. of hematopoietic stem cells or ameliorating one or more of the symptoms of a myeloproliferative disease. Pharmaceutical compns., single unit dosage forms, and kits suitable for use in methods of the invention are also disclosed.
IT 220127-57-1, Imatinib mesylate 220127-57-1D, Imatinib mesylate, derivs.
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(immunomodulators, alone or in combination with other agents, for treatment of myeloproliferative diseases)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

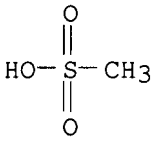
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

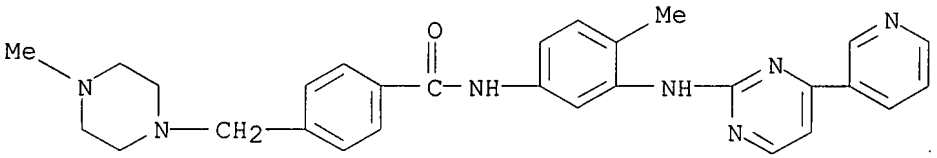
CRN 75-75-2
CMF C H4 O3 S



RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

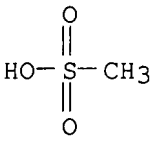
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:1259275 CAPLUS
DN 144:582
TI Methods of using, and compositions comprising, selective cytokine inhibitory drugs for the treatment and management of myeloproliferative diseases
IN Zeldis, Jerome B.
PA Celgene Corporation, USA
SO PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

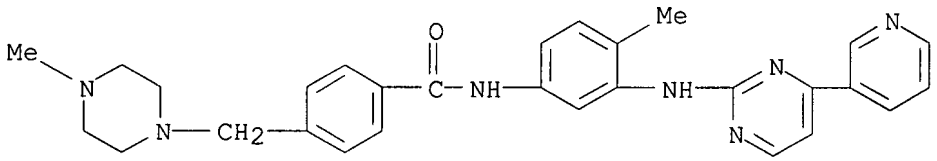
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005112917	A1	20051201	WO 2004-US14001	20040505
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2004319814	A1	20051201	AU 2004-319814	20040505
	CA 2565445	A1	20051201	CA 2004-2565445	20040505
	EP 1746989	A1	20070131	EP 2004-751397	20040505
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, HR, LT, LV, MK				
	CN 1984652	A	20070620	CN 2004-80043536	20040505
	KR 2007007203	A	20070112	KR 2006-725516	20061204
PRAI	WO 2004-US14001	A	20040505		

OS MARPAT 144:582
AB Methods of treating, preventing, and/or managing a myeloproliferative disease are disclosed. Specific methods encompass the administration of a selective cytokine inhibitory drug, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof, alone or in combination with a second active agent, and/or the transplantation of blood or cells. Particular second active agent is capable of suppressing the overprodn. of hematopoietic stem cells or ameliorating one or more of the symptoms of MPD. Pharmaceutical compns., single unit dosage forms, and kits suitable for use in methods of the invention are also disclosed.
IT 220127-57-1, Imatinib mesylate 220127-57-1D, Imatinib mesylate, derivs.
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cytokine inhibitors, alone or in combination with other agents, for treatment of myeloproliferative diseases)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

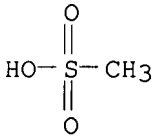
CRN 152459-95-5

CMF C29 H31 N7 O



CM 2

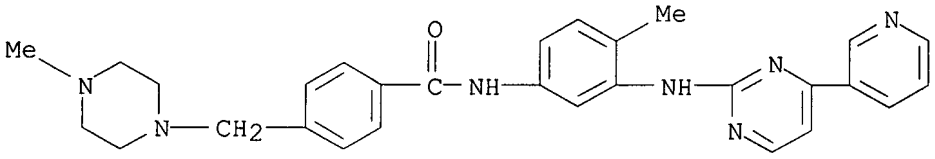
CRN 75-75-2
CMF C H4 O3 S



RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

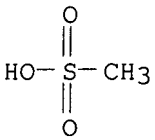
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:1059344 CAPLUS
DN 142:43785
TI Novel polymorphs of imatinib mesylate
IN Parthasaradhi Reddy, Bandi; Rathnakar Reddy, Kura; Raji Reddy, Rapolu; Muralidhara Reddy, Dasari; Subash Chander Reddy, Kesireddy
PA Hetero Drugs Limited, India
SO PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004106326	A1	20041209	WO 2003-IN206	20030602
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IN 194051	A1	20040828	IN 2003-CN851	20030602
IN 2003CN00851	A	20050422		
AU 2003237596	A1	20050121	AU 2003-237596	20030602
TR 200504337	T1	20061221	TR 2005-4337	20030602
IN 2004CH00500	A	20060602	IN 2004-CH500	20040602
US 2005234069	A1	20051020	US 2004-518213	20041216
PRAI WO 2003-IN206	W	20030602		

AB Polymorphs of imatinib mesylate, and processes for their preparation and pharmaceutical compns. containing them is claimed. Imatinib mesylate is prepared from imatinib free base by dissolved in a chlorinated solvent and reacting with methanesulfonic acid. The crystalline form of imatinib mesylate characterized by an X-ray powder diffraction spectrum. Imatinib mesylate hydrate is prepared by dissolving imatinib mesylate in a mixture of a suitable solvent and water and removing the solvents from the solution An example describes the preparation of imatinib mesylate by dissolving imatinib free base (5.0 gm) chloroform (50 mL) at room temperature and then methanesulfonic acid (0.75 mL) is added. The contents are stirred for 5 h at room temperature and separated crystals are filtered and dried to give 5.0 gm of imatinib mesylate form H1.

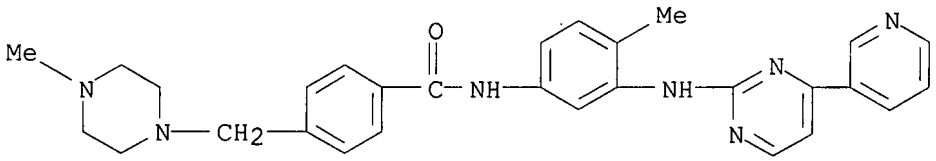
IT 220127-57-1P, Imatinib mesylate
RL: IMF (Industrial manufacture); PRP (Properties); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(polymorphs of imatinib mesylate and preparation of imatinib mesylate hydrates and pharmaceutical compns. containing them)

RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

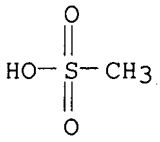
CRN 152459-95-5

CMF C29 H31 N7 O



CM 2

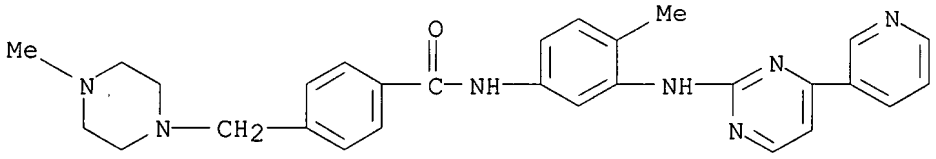
CRN 75-75-2
CMF C H4 O3 S



IT 220127-57-1DP, Imatinib mesylate, hydrate
RL: IMF (Industrial manufacture); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(polymorphs of imatinib mesylate and preparation of imatinib mesylate hydrates and pharmaceutical compns. containing them)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

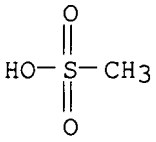
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

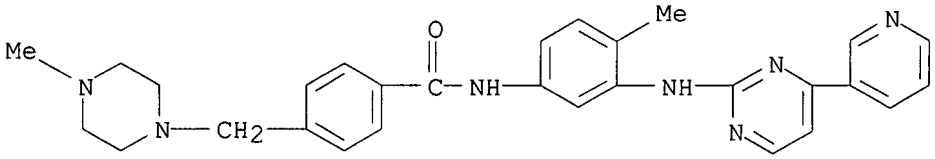
CRN 75-75-2
CMF C H4 O3 S



IT 152459-95-5, Imatinib
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); RCT (Reactant); PROC (Process); RACT (Reactant or reagent)
(polymorphs of imatinib mesylate and preparation of imatinib mesylate hydrates and pharmaceutical compns. containing them)

RN 152459-95-5 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)

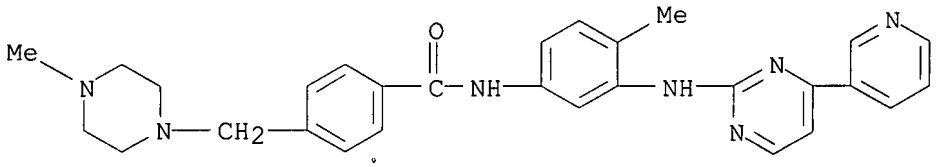


RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:691283 CAPLUS
DN 141:207230
TI Preparation of imatinib and salts by reaction of N-(2-methyl-5-aminophenyl-4-(3-pyridyl)-2-pyrimidinamine with 4-(4-methylpiperazinylmethyl)benzoyl halides.
IN Kankan, Rajendra Narayanrao; Rao, Dharmaraj Ramachandra
PA Cipla Limited, India
SO Brit. UK Pat. Appl., 34 pp.
CODEN: BAXXDU
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI GB 2398565	A	20040825	GB 2003-3730	20030218
AU 2004213616	A2	20040902	AU 2004-213616	20040108
AU 2004213616	A1	20040902		
CA 2516370	A1	20040902	CA 2004-2516370	20040108
WO 2004074502	A2	20040902	WO 2004-GB18	20040108
WO 2004074502	A3	20041028		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1599462	A2	20051130	EP 2004-700728	20040108
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2004007672	A	20060301	BR 2004-7672	20040108
JP 2006518360	T	20060810	JP 2006-502181	20040108
IN 2005MN00950	A	20051202	IN 2005-MN950	20050825
US 2006173182	A1	20060803	US 2005-546193	20051031
PRAI GB 2003-3730	A	20030218		
WO 2004-GB18	A	20040108		

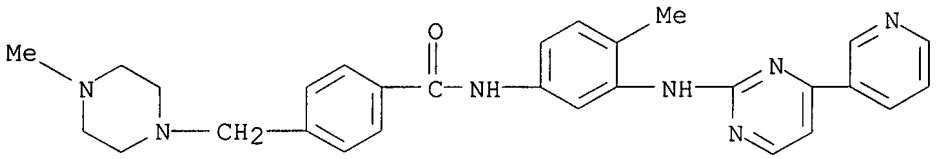
OS CASREACT 141:207230
AB Imatinib and acid addition salts, were prepared by reaction of N-(2-methyl-5-aminophenyl)-4-(3-pyridyl)-2-pyrimidine amine with 4-(4-methylpiperazinylmethyl)benzoyl halides in the presence of an inert organic solvent, to yield a hydrohalide salt of imatinib either in anhydrous or hydrated form, which can be further converted either to the free base or a further acid addition salt.
IT 152459-95-5P, Imatinib 220127-57-1P, Imatinib mesylate 744256-04-0P 744256-05-1P 744256-06-2P
RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of imatinib and salts by reaction of methylaminophenylpyridylpyrimidinamine with methylpiperazinylmethylbenzoyl halides)
RN 152459-95-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

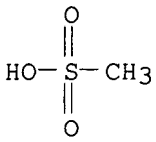
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O

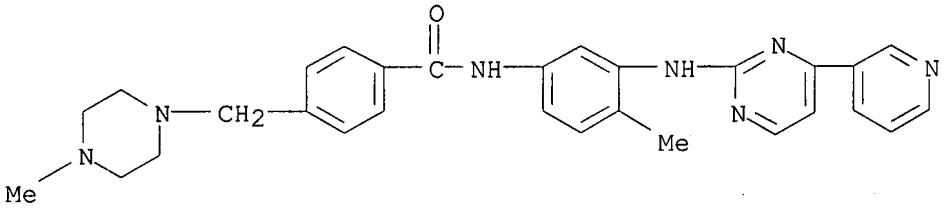


CM 2

CRN 75-75-2
CMF C H4 O3 S

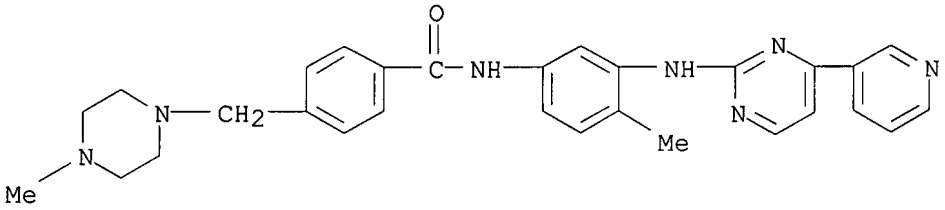


RN 744256-04-0 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, hydrobromide (9CI) (CA INDEX NAME)



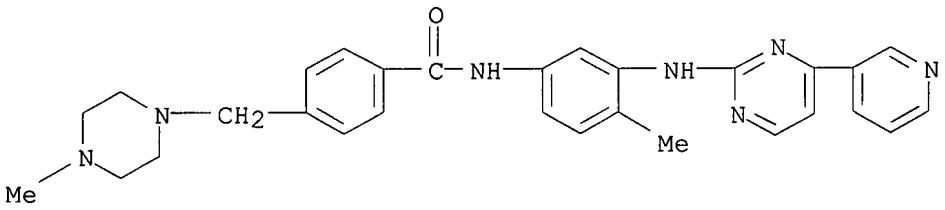
● x HBr

RN 744256-05-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, hydrochloride (9CI) (CA INDEX NAME)



● x HCl

RN 744256-06-2 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, trihydrochloride, monohydrate (9CI) (CA INDEX NAME)



● 3 HCl

● H_2O

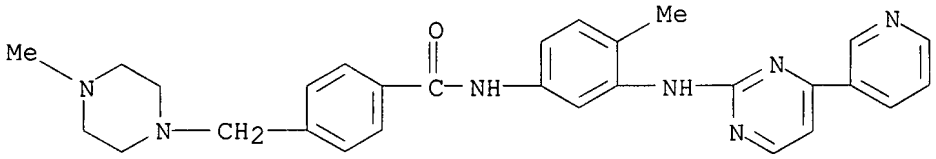
L14 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:430683 CAPLUS
DN 140:417943
TI Methods of using and compositions comprising selective cytokine inhibitory drugs for the treatment and management of myeloproliferative diseases
IN Zeldis, Jerome B.
PA Celgene Corporation, USA
SO PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004043336	A2	20040527	WO 2003-US11325	20030413
	WO 2004043336	A3	20040729		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2505003	A1	20040527	CA 2003-2505003	20030413
	AU 2003226361	A1	20040603	AU 2003-226361	20030413
	EP 1569903	A2	20050907	EP 2003-811178	20030413
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	BR 2003016002	A	20050913	BR 2003-16002	20030413
	CN 1720226	A	20060111	CN 2003-825763	20030413
	JP 2006507324	T	20060302	JP 2004-551394	20030413
	ZA 2005003653	A	20060830	ZA 2005-3653	20030413
	MX 2005PA04777	A	20050722	MX 2005-PA4777	20050504
	US 2006165649	A1	20060727	US 2006-534324	20060224
PRAI	US 2002-424731P	P	20021106		
	WO 2003-US11325	W	20030413		

OS MARPAT 140:417943
AB Methods of treating, preventing and/or managing a myeloproliferative disease (MPD) are disclosed. Specific methods encompass the administration of a selective cytokine inhibitory drug, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof, alone or in combination with a second active agent, and/or the transplantation of blood or cells. Particular second active agent is capable of suppressing the overprodn. of hematopoietic stem cells or ameliorating one or more of the symptoms of MPD. Pharmaceutical compns., single unit dosage forms, and kits suitable for use in methods of the invention are also disclosed.
IT 220127-57-1, Imatinib mesylate
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as second active agent; selective cytokine inhibitory drugs for treatment and management of myeloproliferative diseases)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

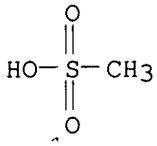
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



```
=> s polymorph? or amorph?
        216069 POLYMORPH?
        280764 AMORPH?
L15     494524 POLYMORPH? OR AMORPH?

=> s l8 and l15
L16         72 L8 AND L15

=> s l16 not l14
L17         71 L16 NOT L14

=> d l17 1-71 bib,ab,hitstr
```

L17 ANSWER 1 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:941813 CAPLUS
DN 147:274950
TI Cancer-associated mutations and polymorphisms of ERBB2, and methods of diagnostic and therapeutic uses
IN Culver, Kenneth Wayne; Zhu, Jian; Lilleberg, Stan
PA Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SO PCT Int. Appl., 99pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007095038	A2	20070823	WO 2007-US3305	20070207

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2006-771907P P 20060209

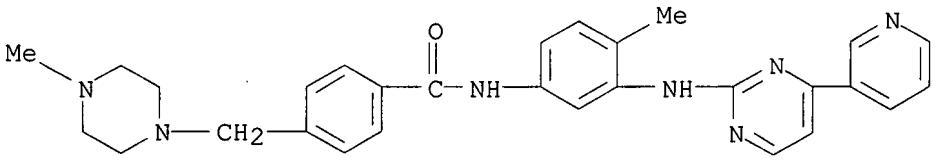
AB This invention relates generally to the anal. testing of tissue samples in vitro, and more particularly to aspects of genetic polymorphisms and mutations of the ERBB2 gene. The invention provides new ERBB2 mutations and SNPs (single nucleotide polymorphisms), useful in the diagnosis and treatment of subjects in need thereof. Accordingly, the various aspects of the present invention relate to polynucleotides encoding the ERBB2 mutations of the invention, expression vectors encoding the ERBB2 mutant polypeptides of the invention and organisms that express the ERBB2 mutant and polymorphic polynucleotides and/or ERBB2 mutant/polymorphic polypeptides of the invention. The various aspects of the present invention further relate to diagnostic/theranostic methods and kits that use the ERBB2 mutations and polymorphisms of the invention to identify individuals predisposed to disease or to classify individuals with regard to drug responsiveness, side effects, or optimal drug dose.

IT 220127-57-1, Glivec
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cancer-associated mutations and polymorphisms of ERBB2, and methods of diagnostic and therapeutic uses)

RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

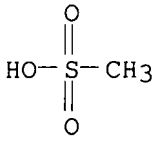
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



L17 ANSWER 2 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:941812 CAPLUS
TI Single nucleotide polymorphisms in PTK2B gene associated with cancer and diagnostic and therapeutic applications
IN Culver, Kenneth Wayne; Zhu, Jian; Lilleberg, Stan
PA Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SO PCT Int. Appl., 85pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007095032	A2	20070823	WO 2007-US3280	20070207

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2006-771775P P 20060209

AB This invention relates generally to the anal. testing of tissue samples in vitro, and more particularly to genotyping single nucleotide polymorphisms in the protein tyrosine kinase 2β (PTK2B) gene associated with increased susceptibility for cancer and methods for diagnosis and therapy. The various aspects of the present invention further relate to diagnostic and therapeutic methods and kits that use the PTK2B mutations and polymorphisms of the invention to identify individuals predisposed to disease or to classify individuals with regard to drug responsiveness, side effects, or optimal drug dose. Cancer may include breast cancer, genitourinary cancer, ovarian cancer, lung cancer, non-small-cell lung cancer (NSCLC), prostate cancer, gastric cancer, gastrointestinal cancer, colon cancer, bladder cancer, renal cancer, pancreas cancer, glioblastoma, glioma, astrocytoma, melanoma, cholangioma, epidermoid cancer, neuroblastoma, head cancer, neck cancer, brain cancer, gastrinomas, adenocarcinoma, oral squamous cell carcinoma, urothelial carcinomas, squamous cell carcinoma of the uterine cervix, chronic myeloid leukemia (CML), acute myelogenous leukemia (AML), and hyperplasias. Anticancer therapy is selected from the group consisting of Glivec, FEMARA, Sandostatin, LAR, ZOMETA, vatalanib, everolimus, gimatecan, patupilone, midostaurin, pasireotide, LBH589, AEE788 and AMN 107.

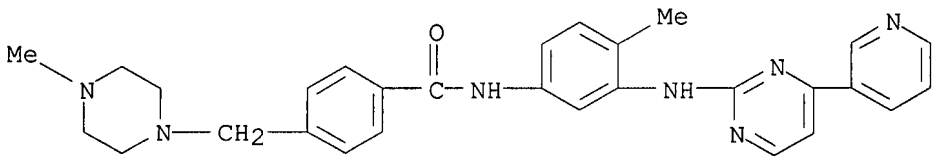
IT 220127-57-1, Glivec
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(single nucleotide polymorphisms in PTK2B gene associated with cancer and diagnostic and therapeutic applications)

RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

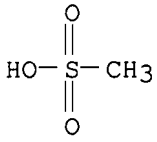
CRN 152459-95-5

CMF C29 H31 N7 O



CM 2

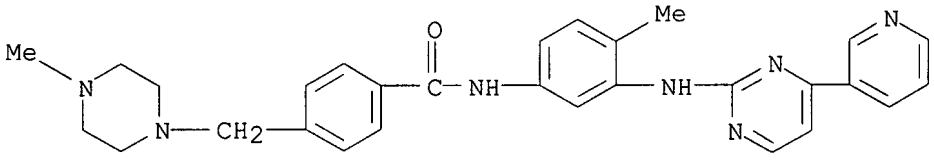
CRN 75-75-2
CMF C H4 O3 S



L17 ANSWER 3 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:916422 CAPLUS
DN 147:225763
TI A review on the relation between the brain-serum concentration ratio of drugs and the influence of P-glycoprotein
AU Ejsing, Thomas Broeng; Morling, Niels; Linnet, Kristian
CS Section of Forensic Chemistry, Institute of Forensic Medicine, Faculty of Health Sciences, University of Copenhagen, Den.
SO Drug Metabolism and Drug Interactions (2006), 22(2-3), 113-129
CODEN: DMDIEQ; ISSN: 0792-5077
PB Freund Publishing House Ltd.
DT Journal; General Review
LA English
AB A review. This overview on the brain-serum relationship for drugs illustrates the importance of the drug transporter P-glycoprotein at the blood-brain barrier. Generally, an inverse relationship exists between the magnitude of the brain-serum ratio and the influence of P-glycoprotein. Concerning the pharmacogenomics of P-glycoprotein, no clear effect of single nucleotide polymorphisms (SNPs) has been demonstrated in humans.
IT 220127-57-1, STI-571
RL: PKT (Pharmacokinetics); BIOL (Biological study)
(review on relation between the brain-serum concentration ratio of drugs and the influence of P-glycoprotein)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

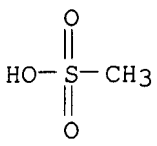
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



L17 ANSWER 4 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:640945 CAPLUS
DN 147:46115
TI Methods of treating cancer and other conditions or disease states using L-cytosine nucleoside analogs
IN Cheng, Yung-Chi
PA Yale University, USA
SO PCT Int. Appl., 48pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

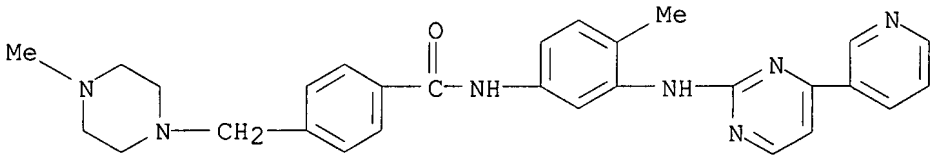
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007067364	A2	20070614	WO 2006-US45270	20061122

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2005-741730P P 20051202
OS MARPAT 147:46115
AB The invention discloses the use of I [S = Q1, Q2; X = H, F; R1 = H, acyl, C1-20 alkyl or ether, a phosphate, diphosphate, triphosphate, phosphodiester, Nu(P(:O)(OR8)O)kP(:O)(OR8), NuC(:O); Nu = radical of biol. active compound such as anticancer, antihyperproliferative or antiviral compound such that an amino group or hydroxyl group from the biol. active agent forms a phosphate, phosphoramidate, carbonate or urethane group with the adjacent moiety; R8 = H, C1-C20 alkyl, ether; k = 0-12; R2 = H, acyl, C1-20 alkyl or ether], and pharmaceutically acceptable salts, solvates or polymorphs thereof for the treatment of tumors, cancer and hyperproliferative diseases, among other conditions or disease states.
IT 220127-57-1, Imatinib mesylate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination; cytosine nucleoside analogs for treatment of cancer or other conditions)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

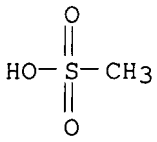
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

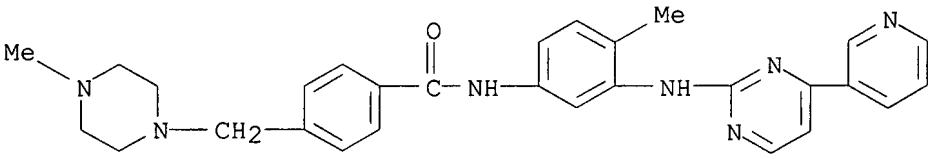
CRN 75-75-2
CMF C H4 O3 S



IT 220127-57-1D, Imatinib mesylate, conjugates with cytosine nucleoside analogs
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cytosine nucleoside analogs for treatment of cancer or other conditions)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

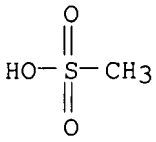
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



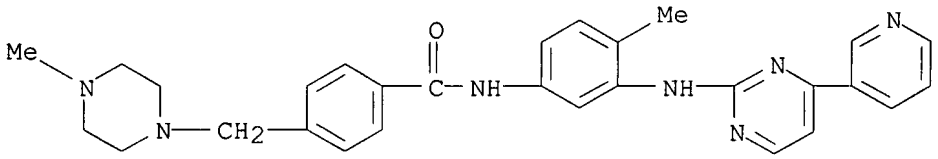
L17 ANSWER 5 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:621707 CAPLUS
DN 147:125684
TI Antitumor composition containing rapamycin, proteinase and/or angiogenesis inhibitor with synergistic interaction
IN Kong, Qingzhong; Su, Hongqing
PA Shandong Lan-Jin Bioengineering Co., Ltd., Peop. Rep. China
SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 23pp.
CODEN: CNXXEV
DT Patent
LA Chinese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	CN 1973822	A	20070606	CN 2006-10201343	20061220
PRAI	CN 2006-10201343		20061220		

AB The title antitumor composition that may be sustained-release injection or implant is composed of (A) sustained-release microsphere comprising effective antitumor component selected from rapamycin, proteinase and/or angiogenesis inhibitor 0.01-60%, sustained-release adjuvant 40-99.99%, and suspending agent 0.0-30%, and (B) solvent that is normal solvent or special solvent containing suspending agent. The angiogenesis inhibitor is selected from gefitinib, erlotinib, lapatinib, etc., or their combination. The suspending agent is selected from sodium CM-cellulose, iodine glycerin, dimethicone, etc., or their combination. The sustained-release adjuvant is selected from poly(lactic acid), poly(glycollic acid), polifeprosan, etc., or their combination, and has good biocompatibility and viscosity of 100-1000 cp (at 20-30°).
IT 220127-57-1, Imatinib mesylate
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor composition containing rapamycin, proteinase and/or angiogenesis inhibitor with synergistic interaction)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

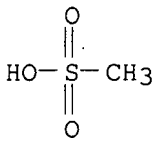
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



L17 ANSWER 6 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:618533 CAPLUS
DN 147:72742
TI Pyrazole urea compounds useful in the treatment of cancer and their preparation
IN Smith, Roger; Hatoum-Mokdad, Holia N.; Cantin, Louis-David; Bierer, Donald E.; Fu, Wenlang; Nagarathnam, Dhanapalan; Ladouceur, Gaetan; Wang, Yamin; Ogutu, Herbert; Wilhelm, Scott; Taylor, Ian; Reddy, Sanjeeva; Gedrich, Richard; Carter, Chris; Schmitt, Aaron; Zhang, Xiaomei
PA Bayer Pharmaceuticals Corporation, USA
SO PCT Int. Appl., 209pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2007064872	A2	20070607	WO 2006-US45976	20061201
	WO 2007064872	A3	20070809		

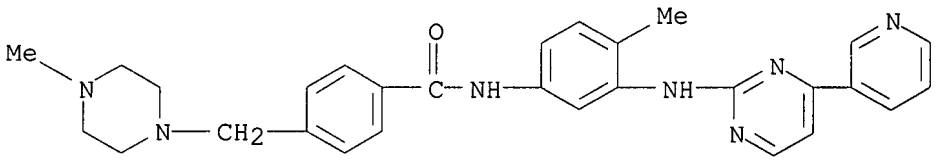
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRAI	US 2005-741052P	P	20051201
	US 2006-861703P	P	20061130

OS MARPAT 147:72742
AB Pyrazole urea compds., of formula I pharmaceutical compns. which contain them and methods for treating cancer using them. Compds. of formula I wherein A is (un)substituted (hetero)aryl; L is S and O bound to the 4 or 5 position of pyridyl; R1 is (un)branched C3-6 alkyl, C3-6 cycloalkyl, Me-substituted C3-5 cycloalkyl, CF3 and C1-3 alkylphenyl; R2 is H and Me; R3 and R4 are independently H and C1-6 alkyl; R5, R6 and R7 are independently H, halo, OH, C1-6 alkyl, C1-5 haloalkyl and C1-3 alkoxy, where at least one of R5, R6 and R7 is H; and their pharmaceutically acceptable salts, metabolites, solvates, hydrates, prodrugs, polymorphs, diastereoisomers, stereoisomers and mixture of stereoisomers thereof, are claimed. Example compound II was prepared by addition of 4-(4-amino-3-fluorophenoxy)-N-methylpyridine-2-carboxamide to [3-benzyl-1-(3-fluorophenyl)-1H-pyrazol-5-yl]carbamate. All the invention compds. were evaluated for their anticancer activity. From the assay, it was determined that the invention compds. exhibited IC50 < 10 μM.
IT 220127-57-1, Gleevec
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of pyrazole urea compds. useful in treatment of cancer)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

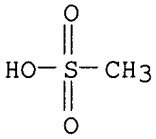
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



L17 ANSWER 7 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:585333 CAPLUS
DN 147:16553
TI Crystal forms of imatinib mesylate and dosage forms containing them for tumor diagnosis and therapy
IN Mutz, Michael
PA Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SO PCT Int. Appl., 43pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007059963	A1	20070531	WO 2006-EP11240	20061123

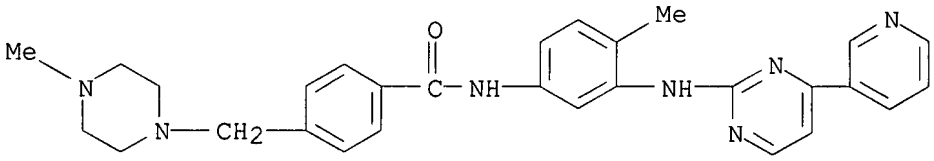
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI GB 2005-24061	A	20051125	
GB 2005-24062	A	20051125	
US 2005-740016P	P	20051128	
US 2005-740017P	P	20051128	
US 2005-740018P	P	20051128	

AB The invention relates to the F-, G-, H-, I-, and K-crystal forms of the methanesulfonic acid addition salt of 4-(4-methylpiperazin-1-yl-methyl)-N-[4-methyl-3-(4-(pyridin-3-yl)pyrimidin-2-yl-amino)phenyl]-benzamide (imatinib), certain processes for their preparation, pharmaceutical compns. containing these crystal forms, their use in diagnostic methods or for the therapeutic treatment of warm-blooded animals, especially humans. Thus, crystalline form F of imatinib mesylate was prepared using benzyl alc. or a mixture of benzyl alc. and Et acetate and formulated into tablets. Tablets containing 100 mg of imatinib mesylate crystal form F were prepared by a direct compression of a mixture containing active ingredient 100 mg, crystalline lactose 240 mg, Avicel 80 mg, PVPPXL 20 mg, Aerosil 2 mg, and magnesium stearate 5 mg.
IT 220127-57-1, Imatinib mesylate
RL: DGN (Diagnostic use); PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(preparation and oral formulations of crystal forms of imatinib mesylate for tumor diagnosis and therapy)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

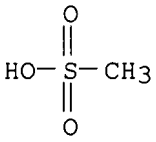
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 8 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:569279 CAPLUS
DN 147:16523
TI New sustained-release microsphere injection formulation of angiogenesis inhibitor and proteinase for cancer therapy
IN Kong, Qingzhong; He, Runping
PA Shandong Lan - Jin Bioengineering Co., Ltd., Peop. Rep. China
SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 34pp.
CODEN: CNXXEV
DT Patent
LA Chinese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI CN 1961861	A	20070516	CN 2006-10201184	20061201
PRAI CN 2006-10201184		20061201		

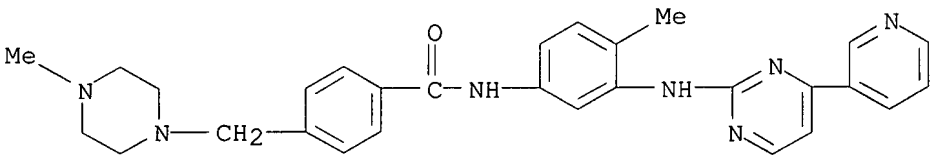
AB The invention provides a new sustained-release microsphere injection formulation of angiogenesis inhibitor and proteinase for cancer therapy. The sustained-release microsphere includes sustained-release adjuvants, angiogenesis inhibitor and/or proteolytic enzyme. The solvent contains suspending agent. Angiogenesis inhibitor is selected from gefitinib, erlotinib, lapatinib, vatalanib, pelitinib, endostatin, imatinib, semaxanib, dasatinib, avastin, sorafenib, telcyta, or panitumumab. Proteolytic enzyme is selected from one or more of collagenase, hyaluronidase, relaxin, and plasmase. The sustained-release adjuvant can be polifeprosan, EVAc, poly(lactic acid), etc. The suspending agent has a viscosity of 100-3000 cp (25 to 30°C), and is selected from sodium CM-cellulose, etc. The sustained-release microsphere can also be manufactured into implant. Intratumoral or peritumoral injection or placement of the sustained-release agent can selectively improve local drug concentration, reduce general reaction to the drug, inhibit cancer cell and blood vessel growth and enhance tumoricidal effect of chemotherapy and/or radiotherapy, and other non-surgical therapies.

IT 220127-57-1, Imatinib mesylate
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(new sustained-release microsphere injection formulation of angiogenesis inhibitor and proteinase for cancer therapy)

RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

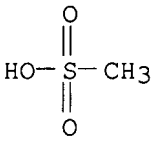
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



L17 ANSWER 9 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:565147 CAPLUS
DN 147:1971
TI Alleles and polymorphisms in the c-abl gene affecting the risk of cancers and the response to chemotherapy
IN Culver, Kenneth Wayne; Zhu, Jian; Lilleberg, Stan
PA Novartis AG, Switz.; Novartis Pharma GmbH
SO PCT Int. Appl., 73pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007058991	A2	20070524	WO 2006-US43898	20061113

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

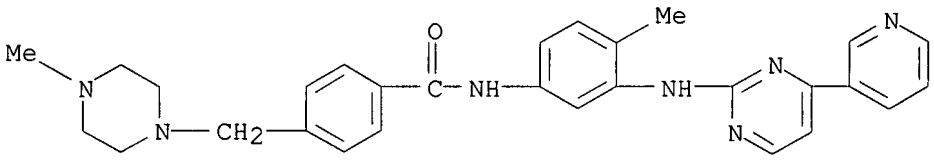
PRAI US 2005-736592P P 20051114

AB Alleles and polymorphisms in the c-abl gene that can affect the risk an individual has of developing certain cancers and in predicting their response to cancer chemotherapy are described.

IT 220127-57-1, Glivec
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(selection for cancer therapy of; alleles and polymorphisms in c-abl gene affecting risk of cancers and response to chemotherapy)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

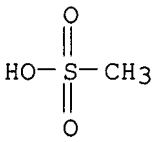
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



L17 ANSWER 10 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:561736 CAPLUS
DN 147:1990
TI Alleles and polymorphisms in the gene for histone deacetylase 6 affecting the risk of cancers and response to chemotherapy
IN Culver, Kenneth Wayne; Zhu, Jian; Lilleberg, Stan
PA Novartis AG, Switz.; Novartis Pharma GmbH
SO PCT Int. Appl., 97pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

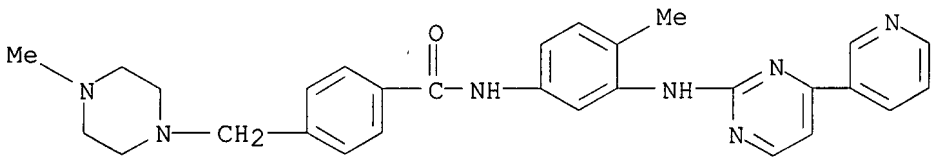
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007058992	A2	20070524	WO 2006-US43899	20061113
WO 2007058992	A3	20070712		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRAI US 2005-736455P P 20051114
OS MARPAT 147:1990
AB Alleles and polymorphisms in the HDAC6 for histone deacetylase 6 that can affect the risk an individual has of developing certain cancers and in predicting their response to cancer chemotherapy are described.
IT 220127-57-1, Glivec
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(selection for cancer therapy of; alleles and polymorphisms in gene for histone deacetylase 6 affecting risk of cancers and response to chemotherapy)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

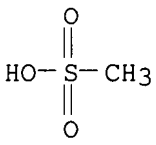
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



L17 ANSWER 11 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:538168 CAPLUS
DN 146:514721
TI Development of DNA microarray for detecting BCR-ABL chimeric gene mutation in chronic myelocytic leukemia and application to the selection of effective drugs
IN Naoe, Tomoki; Yoshida, Yasuko; Yamada, Kazunari; Niwa, Kousuke
PA National University Corp. Nagoya University, Japan; Ngk Insulators, Ltd.
SO PCT Int. Appl., 53pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007055244	A1	20070518	WO 2006-JP322280	20061108

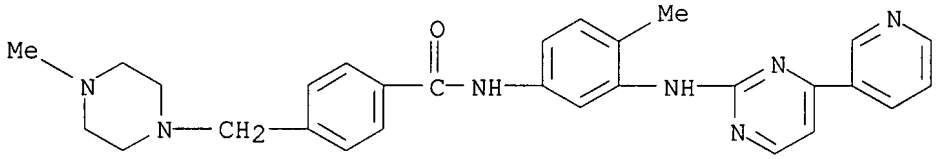
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2005-734278P P 20051108

AB A DNA hybridization microarray system for detecting BCR-ABL chimeric gene mutation in Philadelphia chromosome associated with chronic myelocytic leukemia and drug-sensitivity has been developed. The mutations occurred posteriori and the SNPs cause amino acid alternations at the region corresponding to the kinase domain. Specific 31 SNPs causing amino acid alternation at positions 252, 315 (T→I), etc. are claimed. Combinations of the first group (normal sequences) of probe spots with the second group (SNP sequences) of probe spots that enable to accurately detect the gene mutations by the Nearest Neighbor Method have been claimed. The microarray assay system is more specifically applied to the diagnosis to determine the sensitivities to the drugs such as imatinib, AMN107, BMS-354825, NS-187, ONO12380 and VX-680 and their salts. The anal. is operated by using computer program for selecting the drugs that may be potentially effective in the chemotherapy in individual patients with specific mutations.

IT 152459-95-5, Imatinib 220127-57-1, Imatinib mesylate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(development of DNA microarray for detecting BCR-ABL chimeric gene mutation in chronic myelocytic leukemia and application to selection of effective drugs)

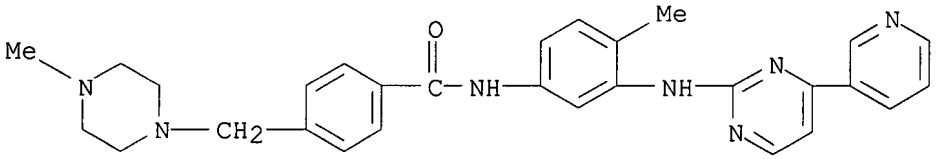
RN 152459-95-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

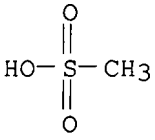
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 12 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:512138 CAPLUS
DN 146:494731
TI Mutations and polymorphisms of human histone deacetylase 5 gene HDAC5 related to diagnosis and treatment of associated diseases
IN Culver, Kenneth Wayne; Zhu, Jian; Lilleberg, Stan
PA Novartis AG, Switz.; Novartis Pharma GmbH
SO PCT Int. Appl., 111pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

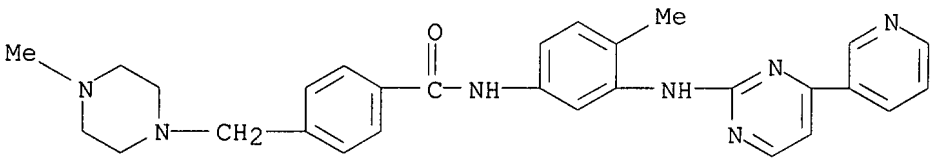
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007053502	A2	20070510	WO 2006-US42187	20061030

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2005-732372P P 20051101
OS MARPAT 146:494731
AB This invention relates generally to the anal. testing of tissue samples in vitro, and more particularly to aspects of genetic polymorphisms and mutations of the human histone deacetylase 5 (HDAC5) gene. The invention provides four new HDAC5 mutations and SNPs found in patients with acute myeloid leukemia, useful in the diagnosis and treatment of subjects in need thereof. Accordingly, the various aspects of the present invention relate to polynucleotides encoding the HDAC5 mutations of the invention, expression vectors encoding the HDAC5 mutant polypeptides of the invention and organisms that express the HDAC5 mutant, and polymorphic polynucleotides and/or HDAC5 mutant/ polymorphic polypeptides of the invention. The various aspects of the present invention further relate to diagnostic/therapeutic methods and kits that use the HDAC5 mutations and polymorphisms of the invention to identify individuals predisposed to disease or to classify individuals with regard to drug responsiveness, side effects, or optimal drug dose.
IT 220127-57-1, Glivec
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anticancer therapy; mutations and polymorphisms of human histone deacetylase 5 gene HDAC5 related to diagnosis and treatment of associated diseases)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

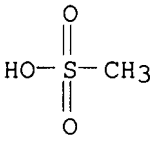
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



L17 ANSWER 13 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:464408 CAPLUS
DN 146:456450
TI Mutations of human histone deacetylase HDAC2 and methods for disease diagnosis and treatment
IN Culver, Kenneth Wayne; Zhu, Jian; Lilleberg, Stan
PA Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SO PCT Int. Appl., 88pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007047998	A2	20070426	WO 2006-US41168	20061019

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2005-728822P P 20051021

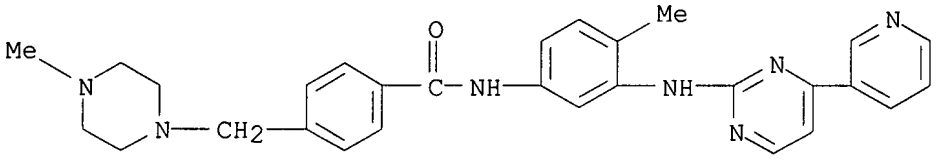
AB This invention relates generally to the anal. testing of tissue samples in vitro, and more particularly to aspects of genetic polymorphisms and mutations of the HDAC2 gene. The invention provides new HDAC2 mutations and SNPs, useful in the diagnosis and treatment of subjects in need thereof. Accordingly, the various aspects of the present invention relate to polynucleotides encoding the HDAC2 mutations of the invention, expression vectors encoding the HDAC2 mutant polypeptides of the invention and organisms that express the HDAC2 mutant and polymorphic polynucleotides and/or HDAC2 mutant/polymorphic polypeptides of the invention. The various aspects of the present invention further relate to diagnostic/theranostic methods and kits that use the HDAC2 mutations and polymorphisms of the invention to identify individuals predisposed to disease or to classify individuals with regard to drug responsiveness, side effects, or optimal drug dose. Thus, two missense mutations in the human HDAC2 gene associated with acute myeloid leukemia are disclosed. These are a GAT>TAT mutation in exon 3 causing a D83Y substitution and a TCA>ACA mutation in exon 4 causing a S118T substitution.

IT 220127-57-1, Glivec
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mutations of human histone deacetylase HDAC2 and methods for disease diagnosis and treatment)

RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

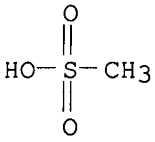
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



L17 ANSWER 14 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:384897 CAPLUS
DN 146:396171
TI Missense mutations of human histone deacetylase gene HDAC11 and methods for cancer diagnosis and treatment
IN Culver, Kenneth Wayne; Zhu, Jian; Lilleberg, Stan
PA Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SO PCT Int. Appl., 90pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

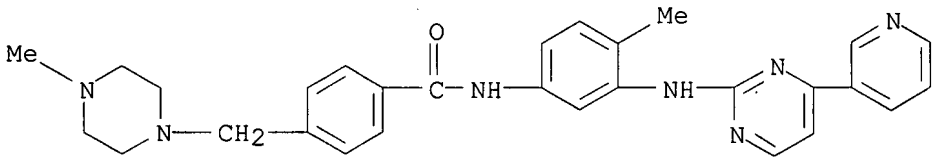
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007038073	A2	20070405	WO 2006-US36421	20060920
WO 2007038073	A3	20070607		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRAI US 2005-719384P P 20050922
OS MARPAT 146:396171
AB The invention provides new human histone deacetylase gene HDAC11 missense mutations useful in the diagnosis and treatment of subjects in need thereof, e.g., cancer patients. Accordingly, the various aspects of the present invention relate to polynucleotides encoding the HDAC11 mutations of the invention, expression vectors encoding the HDAC11 mutant polypeptides of the invention and organisms that express the HDAC11 mutant and polymorphic polynucleotides and/or HDAC11 mutant/ polymorphic polypeptides of the invention. The various aspects of the present invention further relate to diagnostic/theranostic methods and kits that use the HDAC11 mutations and polymorphisms of the invention to identify individuals predisposed to disease or to classify individuals with regard to drug responsiveness, side effects, or optimal drug dose. Thus, the new mutations result in E65A, Q184H, T260S, and M298R amino acid substitutions.
IT 220127-57-1, Glivec
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(missense mutations of human histone deacetylase gene HDAC11 and methods for cancer diagnosis and treatment)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

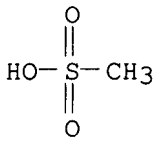
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



L17 ANSWER 15 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:283166 CAPLUS
DN 146:330789
TI Alleles and polymorphisms of histone deacetylase 9 gene HDAC9 and their use in selection of inhibitors for cancer therapy
IN Culver, Kenneth Wayne; Zhu, Jian; Lilleberg, Stan
PA Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SO PCT Int. Appl., 90pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

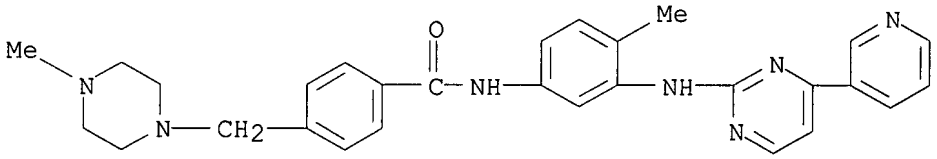
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007030454	A2	20070315	WO 2006-US34559	20060905
WO 2007030454	A3	20070802		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRAI US 2005-714871P P 20050907
OS MARPAT 146:330789
AB New alleles and polymorphisms of the human HDAC9 gene for histone deacetylase 9 that may affect the structure and function of the enzyme are identified for use in the selection of drugs acting on the enzyme. The various aspects of the invention further relate to diagnostic/theranostic methods and kits that use the HDAC9 mutations and polymorphisms of the invention to identify individuals predisposed to disease or to classify individuals with regard to drug responsiveness, side effects, or optimal drug dose. These alleles of the gene may be useful in the diagnosis of disease and in the selection of therapies giving the best response with a min. of side effects.
IT 220127-57-1, Glivec
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as histone deacetylase inhibitor, selection of; alleles and polymorphisms of histone deacetylase 9 gene HDAC9 and their use in selection of inhibitors for cancer therapy)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

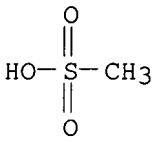
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



L17 ANSWER 16 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:282160 CAPLUS
DN 146:309300
TI Alleles and polymorphisms of the histone deacetylase 10 gene HDAC10 and their use in selection of inhibitors for cancer therapy
IN Culver, Kenneth Wayne; Zhu, Jian; Lilleberg, Stan
PA Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SO PCT Int. Appl., 93pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

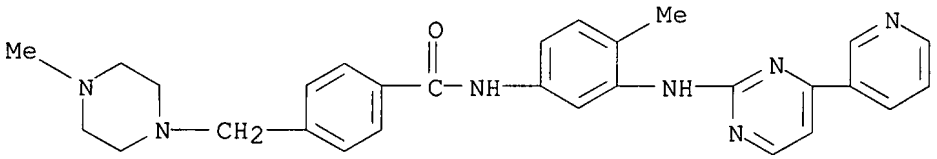
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007030455	A2	20070315	WO 2006-US34561	20060905

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2005-714872P P 20050907
OS MARPAT 146:309300
AB New alleles and polymorphisms of the human HDAC10 gene for histone deacetylase 10 that may affect the structure and function of the enzyme are identified for use in the selection of drugs acting on the enzyme. The various aspects of the present invention further relate to diagnostic/theranostic methods and kits that use the HDAC10 mutations and polymorphisms of the invention to identify individuals predisposed to disease or to classify individuals with regard to drug responsiveness, side effects, or optimal drug dose. These alleles of the gene may be useful in the diagnosis of disease and in the selection of therapies giving the best response with a min. of side effects.
IT 220127-57-1, Glivec
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as histone deacetylase inhibitor, selection of; alleles and polymorphisms of histone deacetylase 10 gene HDAC10 and their use in selection of inhibitors for cancer therapy)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

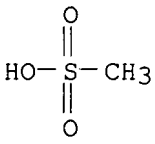
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



L17 ANSWER 17 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:201330 CAPLUS
DN 146:244328
TI Use of histone deacetylase inhibitors to treat proliferative diseases and HDAC3 mutations/polymorphisms in diagnosis of cancer susceptibility
IN Culver, Kenneth Wayne; Zhu, Jian; Lilleberg, Stan
PA Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SO PCT Int. Appl., 80pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

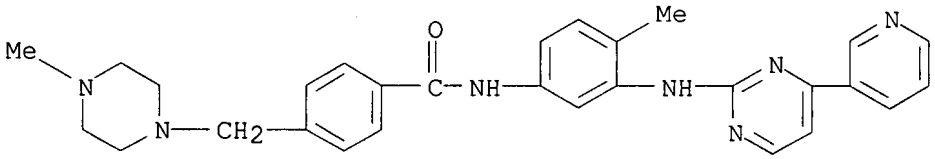
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007022041	A2	20070222	WO 2006-US31560	20060810

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2005-707483P P 20050811
OS MARPAT 146:244328
AB This invention relates generally to the anal. testing of tissue samples in vitro, and more particularly to aspects of genetic polymorphisms and mutations of the HDAC3 gene. The invention provides new HDAC3 mutations and SNPs, useful in the diagnosis and treatment of subjects in need thereof. Thus, if patients are genotyped and found to have the HDAC3 missense mutation of the invention (resulting in truncation of the HDAC3 at K367), they may be treated with acylhydroxamate histone deacetylase inhibitors I (R1,X,Y = H, halo, C1-6-alkyl; R2 = H, C1-10-alkyl, C4-9-cycloalkyl, C4-9-heterocycloalkyl, aryl, hetroaryl, etc.; R3,R4 = H, C1-6-alkyl, acyl, acylamino, or R3 and R4 together with C to which they are attached = C:O, C:S, etc.; R5 = H, C1-6-alkyl, C4-9-cycloalkyl, C4-9-heterocycloalkyl, aryl, acyl, etc.; n = 0-6). The HDAC3 mutation occurred after the histone deacetylase domain and therefore resulted only in the loss of regulatory sites, i.e., tyrosine phosphorylation and sulfation sites and casein kinase II phosphorylation sites.
IT 220127-57-1, Gleevec
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HDAC3 inhibitor and; use of histone deacetylase inhibitors to treat proliferative diseases and HDAC3 mutations and polymorphisms in diagnosis of cancer susceptibility)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

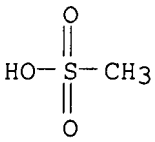
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

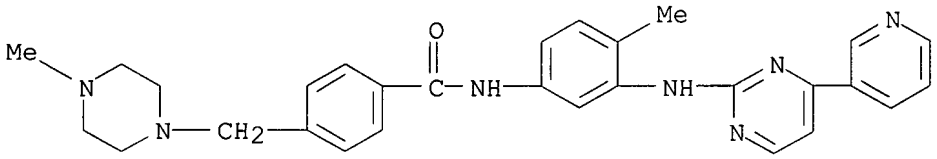
CRN 75-75-2
CMF C H4 O3 S



L17 ANSWER 18 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:196371 CAPLUS
DN 146:330176
TI Oral administration of imatinib to P230 BCR/ABL-expressing transgenic mice changes clones with high BCR/ABL complementary DNA expression into those with low expression
AU Inami, Mitsuharu; Inokuchi, Koiti; Yamaguchi, Hiroki; Nakayama, Kazutaka; Watanabe, Ayako; Uchida, Naoya; Tanosaki, Sakae; Dan, Kazuo
CS Division of Hematology, Department of Third Internal Medicine, Nippon Medical School, Tokyo, Japan
SO International Journal of Hematology (2006), 84(4), 346-353
CODEN: IJHEEY; ISSN: 0925-5710
PB Carden Jennings Publishing
DT Journal
LA English
AB The effect of imatinib on myeloproliferative disease in transgenic (Tg) mice expressing the P230 BCR/ABL transcript is unknown. To investigate this issue, we administered imatinib (30 mg/kg per day) orally to P230 BCR/ABL-expressing Tg mice for 30 days. Following imatinib administration, the enlarged spleen was significantly reduced to within the normal size range. Infiltrating megakaryocytes in the long-axis section of the spleen were also significantly reduced. However, the cellularity of the bone marrow was not affected. Fluorescence-activated cell-sorting anal. revealed that infiltrating mature granulocytes in the spleen were reduced in number The nos. of infiltrating CD34, CD117, CD61, and CD11b populations were also reduced in immature populations of the spleen. Real-time quant. polymerase chain reaction anal. of mRNA revealed a dramatic reduction in the p230 BCR/ABL transcript for CD34, CD117, CD61, and CD11b populations in both bone marrow cells and spleen cells. Western blotting and immunopptn. anal. also revealed a marked reduction in P230 BCR/ABL protein expression in both bone marrow cells and spleen cells. Thus, imatinib administration had the intriguing effect of replacing clones with high expression of p230 BCR/ABL complementary DNA with clones with very low expression. These data show that imatinib may still be capable of eliminating and eradicating clones with high p230 BCR/ABL expression and healing the disease phenotype in Tg mice. Pluripotent clones with very low p230 BCR/ABL expression still survive as immature CD34, CD117, CD61, and CD11b populations.
IT 220127-57-1, Imatinib mesylate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(imatinib by reducing infiltrating immature CD cells, megakaryocyte and mature granulocyte of spleen, inhibited BCR/ABL tyrosine kinase of transgenic mouse-expressing P230 BCR/ABL)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

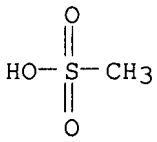
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 19 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:174109 CAPLUS
DN 146:258962
TI Novel salt forms of vildagliptin for therapeutic uses
IN Reber, Jean-Louis; Villhauer, Edwin Bernard
PA Novartis AG, Switz.; Novartis Pharma GmbH
SO PCT Int. Appl., 59pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2007019255	A2	20070215	WO 2006-US30335	20060802
	WO 2007019255	A3	20070531		

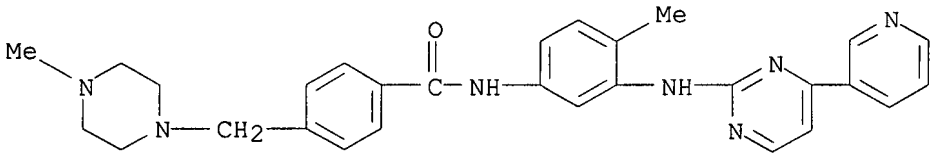
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRAI US 2005-705592P P 20050804

AB The present invention relates to novel salt forms of (S)-1-[(3-hydroxy-1-adamantyl)amino]acetyl-2-cyano-pyrrolidine (LAF237, vildagliptin) and a pharmaceutically acceptable acid in a 1:1 stoichiometry. The salts are in crystalline, partially crystalline, amorphous or polymorphous forms. Thus, 13.0 g of LAF237 was treated with 4.88 g of fumaric acid in ethanol at 50° to afford vildagliptin hydrogen fumarate (yield 17.10 g, 97.1%). The salt showed improved stability compared to vildagliptin base.

IT 152459-95-5, Imatinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination with; preparation and stability of vildagliptin salt forms for treatment of neurodegenerative/cognitive, metabolic and other disorders)

RN 152459-95-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



L17 ANSWER 20 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:150855 CAPLUS
DN 146:226604
TI Use of histone deacetylase inhibitors to treat proliferative diseases and HDAC4 mutations/polymorphisms to diagnose cancer susceptibility
IN Culver, Kenneth Wayne; Zhu, Jian; Lilleberg, Stan
PA Novartis AG, Switz.; Novartis Pharma GmbH
SO PCT Int. Appl., 79pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

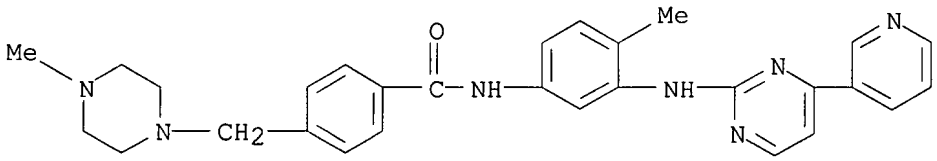
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007016532	A2	20070208	WO 2006-US29851	20060731

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2005-704924P P 20050802
OS MARPAT 146:226604
AB The use of histone deacetylase HDAC4 inhibitors to treat proliferative diseases in patients selected on the basis of the HDAC4 genotype is disclosed. The HDAC4 inhibitor is a hydroxamate compound I (R1 = H, halo, (substituted) C1-C6-alkyl, etc.; R2 = H, C1-C10 alkyl, etc.; R3,R4 = H, C1-C6-alkyl, acyl, acylamino, etc.; R5 = H, C1-C6-alkyl, C4-C9-cycloalkyl, C4-C9-heterocycloalkyl, acyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, aromatic polycycles, nonarom. polycycles, mixed aryl and non-aryl polycycles, polyheteroaryl, nonarom. polyheterocycles, mixed aryl and non-aryl polyheterocycles; X,Y = H, halo, C1-C4-alkyl, NO2, CN, etc.; n1-3 = 0-6). HDAC4 mutations/SNPs associated with susceptibility to proliferative diseases are also disclosed. A method for diagnosing a patients's propensity for developing a proliferative disease based on HDAC4 genotyping is further disclosed. Thus, one HDAC4 substitution mutation was identified in AML patients. This mutation is located in the C-terminus of the HDAC domain of HDAC4. Amino acid changes in the functional domain may alter the protein structure and in turn the protein function and affect response to HDAC inhibitors. AML patients with such mutation may respond to HDAC inhibitors differently from those with wild-type HDAC4 and dictate different clin. outcomes. Thus, this mutation could be potentially used to predict clin. outcomes of HDAC inhibitor in AML patients.
IT 220127-57-1, Glivec
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of histone deacetylase inhibitors to treat proliferative diseases and HDAC4 mutations/polymorphisms to diagnose cancer susceptibility)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

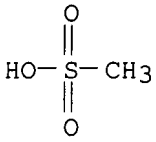
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



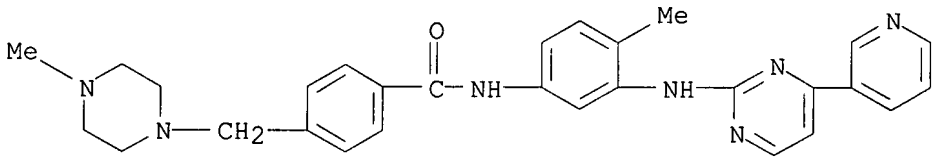
L17 ANSWER 21 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:143469 CAPLUS
DN 146:198711
TI Combination therapy for neurological diseases using c-kit inhibitor and neuroactive compound
IN Chumakov, Ilya; Cohen, Daniel; Macciardi, Fabio
PA Ares Trading S.A., Switz.
SO PCT Int. Appl., 55pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007014943	A2	20070208	WO 2006-EP64870	20060731
WO 2007014943	A3	20070628		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRAI EP 2005-291640	A	20050801	
US 2005-720579P	P	20050926	

AB The present invention relates to novel combination therapies for treating neurol. diseases and more particularly demyelinating diseases (such as multiple sclerosis) in a subject, using a c-kit inhibitor and a neuroactive compound A further aspect of this invention is a method of detecting the presence of or predisposition to a neurol. disease, particularly a demyelinating disease in a subject, the method comprising detecting in vitro or ex vivo the presence or a susceptibility alteration in a c-kit gene or polypeptide in a sample from the subject, the presence of such an alteration being indicative of the presence of or predisposition to a neurol. disease, particularly a demyelinating disease in the subject. The invention also relates to a method of assessing the response or responsiveness of a subject to a treatment of a neurol. disease, particularly a demyelinating disease, the method comprising detecting in vitro or ex vivo the presence of a susceptibility alteration in a c-kit gene or polypeptide in a sample from the subject, the presence of such an alteration being indicative of a responder subject. The present invention originally stems from association studies conducted by the inventors on different MS populations, unexpectedly showing that the c-kit gene is associated with multiple sclerosis and related disorders and that a combined therapeutic approach using neuroactive compds. and c-kit inhibitors provides improved and complementary therapeutic effects in patients.
IT 152459-95-5, Imatinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy with neuroactive compound; combination therapy for neurol. diseases using c-kit inhibitor and neuroactive compound)
RN 152459-95-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



L17 ANSWER 22 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:16764 CAPLUS
DN 146:116033
TI Mutations and polymorphisms of human BCL2 gene proteins and its therapeutic uses
IN Culver, Kenneth Wayne; Zhu, Jian; Lilleberg, Stan
PA Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SO PCT Int. Appl., 64pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007002217	A2	20070104	WO 2006-US24177	20060620

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

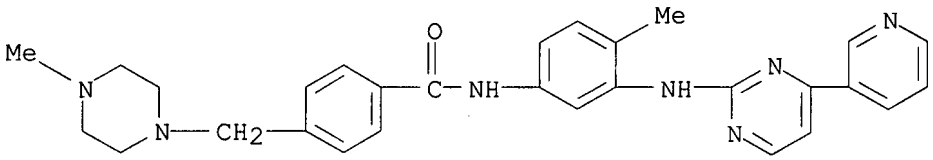
PRAI US 2005-692990P P 20050622

AB This invention relates to the anal. testing of tissue samples in vitro, and new BCL2 mutations and SNPs, useful in the diagnosis and treatment of cancers. The protein sequences of mutant BCL2 proteins have been provided. The invention provides for the use of a BCL2 modulating agent in the manufacture of a medicament for the treatment of cancer in a selected population. Accordingly, the invention relates to polynucleotides encoding the BCL2 mutations of the invention, expression vectors encoding the BCL2 mutant polypeptides of the invention and organisms that express the BCL2 mutant and polymorphic polynucleotides and/or BCL2 mutant/polymorphic polypeptides of the invention. The invention further relate to diagnostic methods and kits that use the BCL2 mutations and polymorphisms of the invention to identify individuals predisposed to disease or to classify individuals with regard to drug responsiveness, side effects, or optimal drug dose.

IT 220127-57-1, Gleevec
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mutations and polymorphisms of human BCL2 gene proteins and its therapeutic uses)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

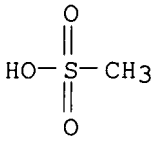
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



L17 ANSWER 23 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1285847 CAPLUS
DN 146:39776
TI Mutations and SNPs of human fibroblast growth factor receptor 1 (FGFR1) gene and methods of use in cancer diagnosis and cancer chemotherapy
IN Culver, Kenneth Wayne; Zhu, Jian; Lilleberg, Stan
PA Novartis AG, Switz.; Novartis Pharma GmbH
SO PCT Int. Appl., 72pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006130527	A2	20061207	WO 2006-US20665	20060330
WO 2006130527	A3	20070726		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

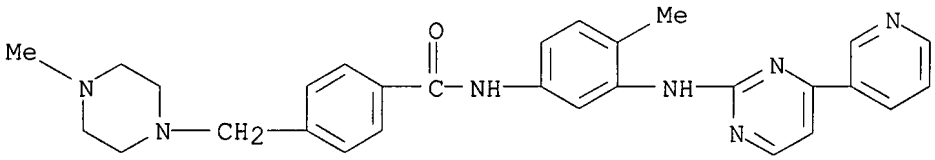
PRAI US 2005-685950P P 20050531

AB This invention relates generally to the anal. testing of tissue samples in vitro, and more particularly to aspects of genetic polymorphisms and mutations of the fibroblast growth factor receptor. The invention provides new FGFR1 mutations and SNPs, useful in the diagnosis and treatment of subjects in need thereof and including cancer patients. Accordingly, the various aspects of the present invention relate to polynucleotides encoding the FGFR1 mutations of the invention, expression vectors encoding the FGFR1 mutant polypeptides of the invention and organisms that express the FGFR1 mutant and polymorphic polynucleotides and/or FGFR1 mutant/polymorphic polypeptides of the invention. The various aspects of the present invention further relate to diagnostic/prognostic methods that use the FGFR1 mutations and polymorphisms of the invention to identify individuals predisposed to disease or to classify individuals with regard to drug responsiveness, side effects, or optimal drug dose.

IT 220127-57-1, Glivec
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mutations and SNPs of human fibroblast growth factor receptor 1 (FGFR1) gene and methods of use in cancer diagnosis and chemotherapy)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

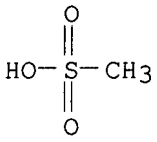
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

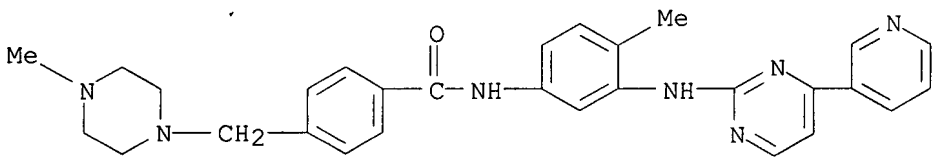
CRN 75-75-2
CMF C H4 O3 S



L17 ANSWER 24 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1170671 CAPLUS
DN 146:38378
TI Selective binding of imatinib to the genetic variants of human α1-acid glycoprotein
AU Fitos, Ilona; Visy, Julia; Zsila, Ferenc; Mady, Gyoergy; Simonyi, Miklos
CS Department of Molecular Pharmacology, Institute of Biomolecular Chemistry Chemical Research Center, Hungarian Academy of Sciences, Budapest, H-1525, Hung.
SO Biochimica et Biophysica Acta, General Subjects (2006), 1760(11), 1704-1712
CODEN: BBGSB3; ISSN: 0304-4165
PB Elsevier Ltd.
DT Journal
LA English
AB Imatinib is a selective tyrosine kinase inhibitor, successfully used for the treatment of chronic myelogenous leukemia. Its strong plasma protein binding referred to α1-acid glycoprotein (AGP) component was found to inhibit the pharmacol. activity. AGP shows genetic polymorphism and the two main genetic variants have different drug binding properties. The binding characteristics of imatinib to AGP genetic variants and the possibility of its binding interactions were investigated by various methods. The results proved that binding of imatinib to the two main genetic variants is very different, the high affinity binding belongs dominantly to the F1-S variant. This interaction is accompanied with specific spectral changes (induced CD, UV change, intrinsic fluorescence quenching), suggesting that the bound ligand has chiral conformation that would largely overlap with other ligands inside the protein cavity. Binding parameters of Ka = 1.7(± 0.2) + 106 M-1 and n = 0.94 could be determined for the binding on the F1-S variant at 37°. Imatinib binding on the A variant is weaker and less specific. The binding affinity of imatinib to human serum albumin (nKa ≈ 3 + 104 M-1) is low. Pharmacol. relevant binding interactions with other drugs can be expected on the F1-S variant of AGP.
IT 220127-57-1, Imatinib mesylate
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(selective binding of imatinib to the genetic variants of human α1-acid glycoprotein)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

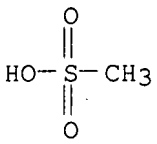
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 25 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1150361 CAPLUS
DN 145:478002
TI Implantable device comprising amorphous poly(D,L-lactide) coating
IN Pacetti, Stephen D.; Hossainy, Syed Faiyaz Ahmed; Gale, David C.
PA USA
SO U.S. Pat. Appl. Publ., 9pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2006246108	A1	20061102	US 2005-117813	20050429
WO 2006118808	A1	20061109	WO 2006-US14889	20060419

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

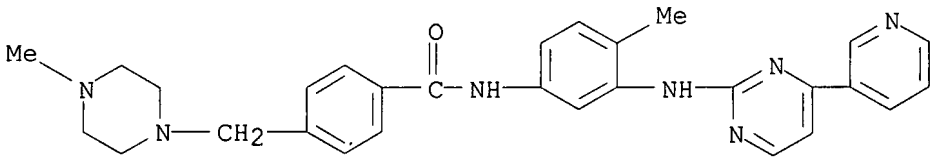
PRAI US 2005-117813 A 20050429

AB Implantable devices formed of or coated with a material that includes an amorphous poly(D,L-lactide) formed of a starting material such as meso-D,L-lactide are provided. The implantable device can be used for the treatment, mitigation, prevention, or inhibition of a disorder such as atherosclerosis, thrombosis, restenosis, hemorrhage, vascular dissection or perforation, vascular aneurysm, vulnerable plaque, chronic total occlusion, patent foramen ovale, claudication, anastomotic proliferation for vein and artificial grafts, bile duct obstruction, ureter obstruction, tumor obstruction, or combinations thereof. Thus, L-lactic acid 125 g, D-lactic acid 125 g, and zinc oxide 5 g was added to 3-necked 500 mL flask, equipped with argon purge, vacuum line, short-path distillation head, and mech. stirrer. A vacuum of 100 mm Hg was applied, and the solution was heated with stirring at 140 °C for about 8 h to form lactic acid oligomer while distilling off the water formed. The pressure was lowered to 2 mm Hg, and the solution temperature raised to about 210 °C to distill off the lactide formed by depolymn., which consists of a 25/25/50 blend of L-lactide, D-lactide, and meso-D,L-lactide. The lactides formed were transferred to another 500 mL flask, and vacuum distilled at a pressure of 1 mm Hg to sep. the racemic-D,L-lactide from the meso-D,L-lactide.

IT 220127-57-1, Imatinib mesylate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(implantable device comprising amorphous poly(D,L-lactide) coating)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

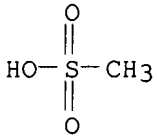
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



L17 ANSWER 26 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1097643 CAPLUS
DN 145:433085
TI Alleles and polymorphisms of the epidermal growth factor receptor gene and their diagnostic uses
IN Culver, Kenneth W.; Zhu, Jian; Lilleberg, Stan
PA Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SO PCT Int. Appl., 118pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006110478	A2	20061019	WO 2006-US12878	20060407
WO 2006110478	A3	20070426		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRAI US 2005-670061P P 20050411

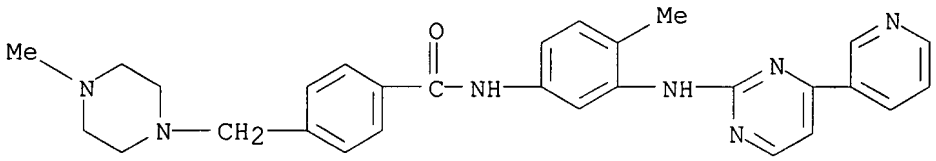
AB Methods for detecting new and previously known alleles and single-nucleotide polymorphisms in the human EGFR gene for epidermal growth factor receptor are described for use in the diagnosis of disease and in the selection of therapies. The invention provides new EGFR mutations and SNPs, useful in the diagnosis and treatment of subjects in need thereof. Accordingly, the various aspects of the present invention relate to polynucleotides encoding the EGFR mutations of the invention, expression vectors encoding the EGFR mutant polypeptides of the invention and organisms that express the EGFR mutant and polymorphic polynucleotides and/or EGFR mutant/polymorphic polypeptides of the invention. The various aspects of the present invention further relate to diagnostic/theranostic methods and kits that use the EGFR mutations and polymorphisms of the invention to identify individuals predisposed to disease or to classify individuals with regard to drug responsiveness, side effects, or optimal drug dose.

IT 220127-57-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(for cancer therapy, gene EGFR alleles in selection of; alleles and polymorphisms of epidermal growth factor receptor gene and their diagnostic uses)

RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

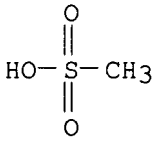
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

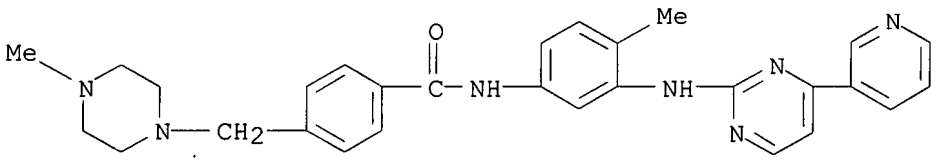
CRN 75-75-2
CMF C H4 O3 S



L17 ANSWER 27 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1051438 CAPLUS
DN 146:408
TI BNP as a marker of the heart failure in the treatment of imatinib mesylate
AU Park, Yeon Hee; Park, Hae Jeong; Kim, Bong-Seog; Ha, Eunyoung; Jung, Kyung Hee; Yoon, Seo Hyun; Yim, Sung Vin; Chung, Joo-Ho
CS Department of Medical Oncology, Korea Institute of Radiological and Medical Sciences, Seoul, 130-706, S. Korea
SO Cancer Letters (Amsterdam, Netherlands) (2006), 243(1), 16-22
CODEN: CALEDQ; ISSN: 0304-3835
PB Elsevier B.V.
DT Journal
LA English
AB Since its introduction 6 years ago, imatinib mesylate, a selective tyrosine kinase inhibitor, has been a phenomenon in treating chronic myelogenous leukemia (CML) with remarkably superior cytogenetic and mol. response rates at all stages of CML followed by longer progression free survival. Despite its extraordinarily high efficacy, adverse effects of imatinib mesylate such as edema, liver toxicity and fluid retention syndromes have been reported. Here we, for the first time, report development of heart failure in patients on imatinib mesylate medication and the possibility of brain natriuretic peptide (BNP) as a potential diagnostic (or predicting) marker for heart failure. Since plasma BNP levels in the two patients were exceptionally high, we then explored the possibility of genetic association of BNP with the development of heart failure to find no pos. association
IT 220127-57-1, Imatinib mesylate
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(BNP as a marker of heart failure in treatment of imatinib mesylate)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

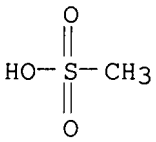
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S

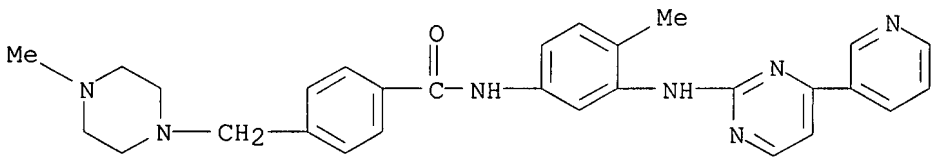


RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 28 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1039164 CAPLUS
DN 145:383558
TI Preparation of crystalline imatinib base
IN Adin, Itai; Futerman, Yuri; Iustain, Carmen
PA Chemagis Ltd., Israel
SO U.S. Pat. Appl. Publ., 8pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006223817	A1	20061005	US 2006-433941	20060515
PRAI US 2006-433941		20060515		

AB Provided is crystalline imatinib base form I and processes for producing crystalline imatinib base form I, which is suitable for preparing imatinib salts such as, e.g., the mesylate salt. Also provided is a process for producing a salt of imatinib from crystalline imatinib base form I. Imatinib was prepared by the reaction of N-(5-amino-2-methylphenyl)-4-(3-pyridyl)-2-pyrimidineamine with 4-(4-methylpiperazinylmethyl)benzoyl chloride in pyridine and purified.
IT 152459-95-5P, Imatinib
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of crystalline imatinib base)
RN 152459-95-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



L17 ANSWER 29 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1039160 CAPLUS
DN 145:383417
TI Preparation of imatinib mesylate α-form
IN Adin, Itai; Iustain, Carmen; Davidi, Guy; Weisman, Alex; Bentolila, Moshe; Meyer, Elazar; Kaspi, Joseph
PA Chemagis Ltd., Israel
SO U.S. Pat. Appl. Publ., 10pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

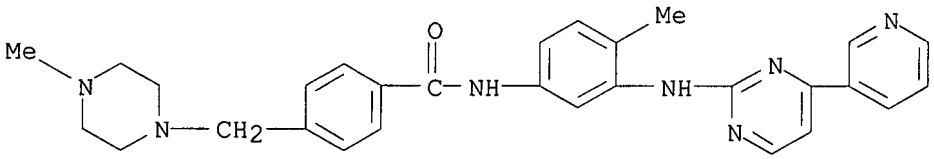
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2006223816	A1	20061005	US 2006-429731	20060508
PRAI US 2006-429731		20060508		

AB Provided is a process for preparing crystalline imatinib mesylate in substantially pure α-form, which preferably includes crystallizing imatinib mesylate from an organic solvent containing imatinib and methanesulfonic acid, and seed crystals of imatinib mesylate α-form, wherein the seed crystals are added before imatinib mesylate begins to precipitate from the mixture Also provided are stable, free-flowing imatinib mesylate crystals in substantially pure α-form, and a pharmaceutical composition containing the stable, free-flowing imatinib mesylate crystals.

IT 220127-57-1P, Imatinib mesylate
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of imatinib mesylate α-form)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

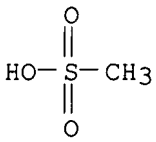
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O

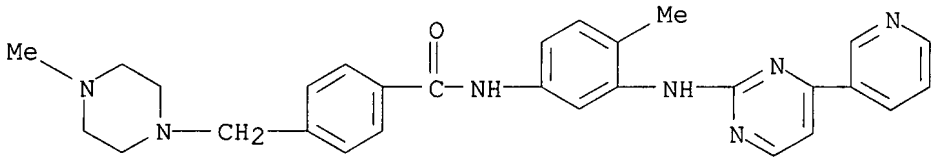


CM 2

CRN 75-75-2
CMF C H4 O3 S



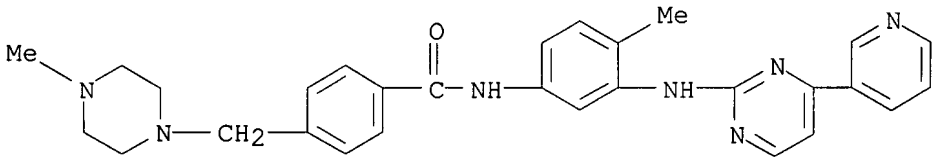
IT 152459-95-5, Imatinib
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(preparation of imatinib mesylate α-form)
RN 152459-95-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



L17 ANSWER 30 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:876420 CAPLUS
DN 146:414205
TI Population pharmacokinetics of imatinib and the role of α1-acid glycoprotein
AU Widmer, N.; Decosterd, L. A.; Csajka, C.; Leyvraz, S.; Duchosal, M. A.; Rosselet, A.; Rochat, B.; Eap, C. B.; Henry, H.; Biollaz, J.; Buclin, T.
CS Division of Clinical Pharmacology, University Hospital, Lausanne, Switz.
SO British Journal of Clinical Pharmacology (2006), 62(1), 97-112
CODEN: BCPHBM; ISSN: 0306-5251
PB Blackwell Publishing Ltd.
DT Journal
LA English
AB Aims: The aims of this observational study were to assess the variability in imatinib pharmacokinetics and to explore the relationship between its disposition and various biol. covariates, especially plasma α1-acid glycoprotein concns. Methods: A population pharmacokinetic anal. was performed using NONMEM based on 321 plasma samples from 59 patients with either chronic myeloid leukemia or gastrointestinal stromal tumors. The influence of covariates on oral clearance and volume of distribution was examined Furthermore, the in vivo intracellular pharmacokinetics of imatinib was explored in five patients. Results: A one-compartment model with first-order absorption appropriately described the data, giving a mean (± SEM) oral clearnace of 14.3 I h-1 (± 1.0) and a volume of distribution of 347 I (± 62). Oral clearance was influenced by body weight, age, sex and disease diagnosis. A large proportion of the interindividual variability (36% of clearance and 63% of volume of distribution) remained unexplained by these demog. covariates. Plasma α1-acid glycoprotein concns. had a marked influence on total imatinib concns. Moreover, we observed an intra/extracellular ratio of 8, suggesting substantial uptake of the drug into the target cells. Conclusion: Because of the high pharmacokinetic variability of imatinib and the reported relationships between its plasma concentration and efficacy and
toxicity, the usefulness of therapeutic drug monitoring as an aid to optimizing therapy should be further investigated. Ideally, such an approach should take account of either circulating α1-acid glycoprotein concns. or free imatinib concns.
IT 220127-57-1, Gleevec
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(high interpatient and limited intrapatient variability in Gleevec-pharmacokinetics and potential relationship between exposure, efficacy, toxicity was observed in patient with gastrointestinal stromal tumor or chronic myeloid leukemia)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

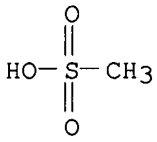
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S

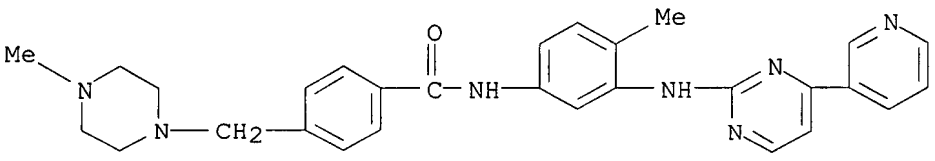


RE.CNT 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 31 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:828589 CAPLUS
DN 145:224511
TI Leukemogenesis induced by wild-type and STI571-resistant BCR/ABL is potently suppressed by C/EBPα
AU Ferrari-Amorotti, Giovanna; Keeshan, Karen; Zattoni, Michela; Guerzoni, Clara; Iotti, Giorgio; Cattelani, Sara; Donato, Nick J.; Calabretta, Bruno
CS Department of Microbiology and Immunology, Kimmel Cancer Center, Thomas Jefferson Medical College, Philadelphia, PA, USA
SO Blood (2006), 108(4), 1353-1362
CODEN: BLOOAW; ISSN: 0006-4971
PB American Society of Hematology
DT Journal
LA English
AB Chronic phase-to-blast crisis transition in chronic myelogenous leukemia (CML) is associated with differentiation arrest and down-regulation of C/EBPα, a transcription factor essential for granulocyte differentiation. Patients with CML in blast crisis (CML-BC) became rapidly resistant to therapy with the breakpoint cluster region-Abelson murine leukemia (BCR/ABL) kinase inhibitor imatinib (STI571) because of mutations in the kinase domain that interfere with drug binding. We show here that the restoration of C/EBPα activity in STI571-sensitive or -resistant 32D-BCR/ABL cells induced granulocyte differentiation, inhibited proliferation in vitro and in mice, and suppressed leukemogenesis. Moreover, activation of C/EBPα eradicated leukemia in 4 of 10 and in 6 of 7 mice injected with STI571-sensitive or -resistant 32D-BCR/ABL cells, resp. Differentiation induction and proliferation inhibition were required for optimal suppression of leukemogenesis, as indicated by the effects of p42 C/EBPα, which were more potent than those of K298E C/EBPα, a mutant defective in DNA binding and transcription activation that failed to induce granulocyte differentiation. Activation of C/EBPα in blast cells from 4 patients with CML-BC, including one resistant to STI571 and BMS-354825 and carrying the T315I Abl kinase domain mutation, also induced granulocyte differentiation. Thus, these data indicate that C/EBPα has potent antileukemia effects even in cells resistant to ATP-binding competitive tyrosine kinase inhibitors, and they portend the development of antileukemia therapies that rely on C/EBPα activation.
IT 220127-57-1, STI571
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(C/EBPα has potent antileukemia effects even in cells resistant to ATP-binding competitive tyrosine kinase inhibitors)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

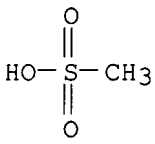
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S

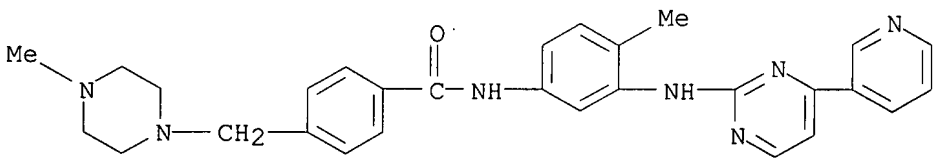


RE.CNT 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 32 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:816353 CAPLUS
DN 146:265703
TI Phase I/II Study of Imatinib Mesylate for Recurrent Malignant Gliomas: North American Brain Tumor Consortium Study 99-08
AU Wen, Patrick Y.; Yung, W. K. Alfred; Lamborn, Kathleen R.; Dahia, Patricia L.; Wang, Yanfeng; Peng, Bin; Abrey, Lauren E.; Raizer, Jeffrey; Cloughesy, Timothy F.; Fink, Karen; Gilbert, Mark; Chang, Susan; Junck, Larry; Schiff, David; Lieberman, Frank; Fine, Howard A.; Mehta, Minesh; Robins, H. Ian; DeAngelis, Lisa M.; Groves, Morris D.; Puduvalli, Vinay K.; Levin, Victor; Conrad, Charles; Maher, Elizabeth A.; Aldape, Kenneth; Hayes, Michael; Letvak, Laurie; Egorin, Merrill J.; Capdeville, Renaud; Kaplan, Richard; Murgo, Anthony J.; Stiles, Charles; Prados, Michael D.
CS Dana-Farber/Brigham and Women's Cancer Center, Boston, MA, 02115, USA
SO Clinical Cancer Research (2006), 12(16), 4899-4907
CODEN: CCREF4; ISSN: 1078-0432
PB American Association for Cancer Research
DT Journal
LA English
AB PURPOSE: Phase I: To determine the maximum tolerated doses, toxicities, and pharmacokinetics of imatinib mesylate (Gleevec) in patients with malignant gliomas taking enzyme-inducing antiepileptic drugs (EIAED) or not taking EIAED. Phase II: To determine the therapeutic efficacy of imatinib. Exptl. Design: Phase I component used an inter-patient dose escalation scheme. End points of the phase II component were 6-mo progression-free survival and response. RESULTS: Fifty patients enrolled in the phase I component (27 EIAED and 23 non-EIAED). The maximum tolerated dose for non-EIAED patients was 800 mg/d. Dose-limiting toxicities were neutropenia, rash, and elevated alanine aminotransferase. EIAED patients received up to 1200 mg/d imatinib without developing dose-limiting toxicity. Plasma exposure of imatinib was reduced by .apprx.68% in EIAED patients compared with non-EIAED patients. Fifty-five non-EIAED patients (34 glioblastoma multiforme and 21 anaplastic glioma) enrolled in the phase II component. Patients initially received 800 mg/d imatinib; 15 anaplastic glioma patients received 600 mg/d after hemorrhages were observed There were 2 partial response and 6 stable disease among glioblastoma multiforme patients and 0 partial response and 5 stable disease among anaplastic glioma patients. Six-month progression-free survival was 3% for glioblastoma multiforme and 10% for anaplastic glioma patients. Five phase II patients developed intratumoral hemorrhages. CONCLUSIONS: Single-agent imatinib has minimal activity in malignant gliomas. CYP3A4 inducers, such as EIAEDs, substantially decreased plasma exposure of imatinib and should be avoided in patients receiving imatinib for chronic myelogenous leukemia and gastrointestinal stromal tumors. The evaluation of the activity of combination regimens incorporating imatinib is under way in phase II trials.
IT 220127-57-1, Gleevec
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(maximum tolerated doses, toxicities, and pharmacokinetics of imatinib mesylate (Gleevec) in patients with malignant gliomas taking enzyme-inducing antiepileptic drugs (EIAED) or not taking EIAED)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

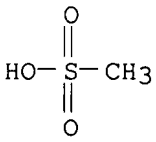
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S

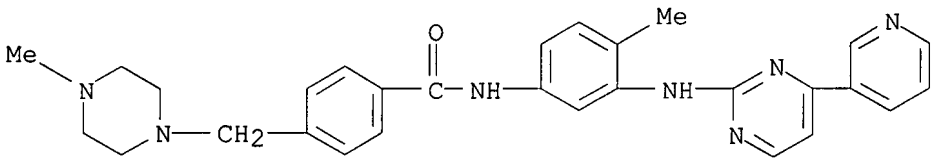


RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 33 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:816253 CAPLUS
DN 146:243174
TI Association of enzyme and transporter genotypes with the pharmacokinetics of imatinib
AU Gardner, Erin R.; Burger, Herman; van Schaik, Ron H.; van Oosterom, Allan T.; de Bruijn, Ernst A.; Guetens, Gunther; Prenen, Hans; de Jong, Floris A.; Baker, Sharyn D.; Bates, Susan E.; Figg, William D.; Verweij, Jaap; Sparreboom, Alex; Nooter, Kees
CS Clinical Pharmacology Research Core, SAIC-Frederick, Frederick, MD, USA
SO Clinical Pharmacology & Therapeutics (New York, NY, United States) (2006), 80(2), 192-201
CODEN: CLPTAT; ISSN: 0009-9236
PB Elsevier
DT Journal
LA English
AB Objective: Our objective was to explore the relationships between imatinib pharmacokinetics and 9 allelic variants in 7 genes coding for ATP-binding cassette transporters (ABCB1 and ABCG2) and enzymes (cytochrome P 450 [CYP] 2C9, CYP2C19, CYP2D6, CYP3A4, and CYP3A5) of putative relevance for imatinib. Methods: Imatinib transport in vitro was studied by use of human embryonic kidney 293 cells transfected with wild-type ABCG2 and an ABCG2 Q141K clone. Steady-state pharmacokinetics of imatinib was obtained in 82 patients with gastrointestinal stromal tumors treated with oral imatinib at doses ranging from 100 to 1000 mg/d. Genotyping was carried out via direct sequencing or restriction fragment length polymorphism-based techniques. Results: Human embryonic kidney 293 cells transfected with ABCG2 Q141K exhibited greater drug accumulation in vitro in comparison with cells expressing wild-type ABCG2 (P =.028). However, pharmacokinetic parameters of imatinib in vivo were not statistically significantly different in 16 patients who were heterozygous for ABCG2 421C>A compared with 66 patients carrying the wild-type sequence (P =.479). The apparent oral clearance of imatinib was potentially reduced in individuals with at least 1 CYP2D6*4 allele (median, 7.78 vs. 10.6 L/h; P =.0695). Pharmacokinetic parameters were not related to any of the other multiple-variant genotypes (P ≥.230), possibly because of the low allele frequencies. Conclusions: This study indicates that common genetic variants in the evaluated genes have only a limited impact on the pharmacokinetics of imatinib. Further investigation is required to quant. assess the clin. significance of homozygous variant ABCG2 and CYP2D6 genotypes in patients treated with imatinib.
IT 220127-57-1, Gleevec
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(allelic variants in CYP2C9, CYP2C19, CYP2D6, CYP3A4, CYP3A5, ABCB1 and ABCG2 genes showed limited impact on interindividual variability in Gleevec pharmacokinetics in gastrointestinal stromal tumor patient)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

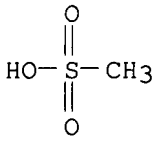
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



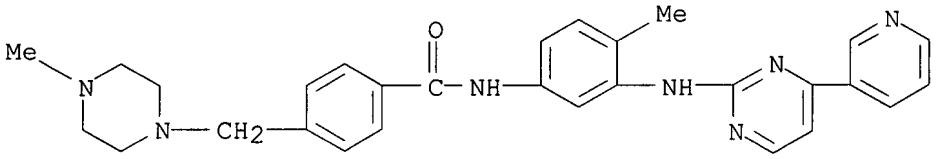
CM 2

CRN 75-75-2
CMF C H4 O3 S



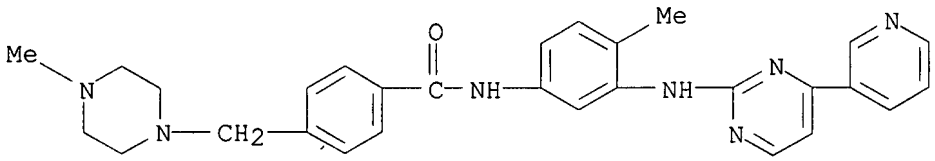
RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 34 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:560869 CAPLUS
DN 145:410173
TI The effects of saquinavir on imatinib-resistant chronic myelogenous leukemia cell lines
AU Timeus, Fabio; Crescenzio, Nicoletta; Ricotti, Emanuela; Doria, Alessandra; Bertin, Daniele; Saglio, Giuseppe; Tovo, Pier Angelo
CS Department of Onco-hematology and Immunology, University of Turin, Italy
SO Haematologica (2006), 91(5), 711-712
CODEN: HAEMAX; ISSN: 0390-6078
PB Ferrata Storti Foundation
DT Journal
LA English
AB We evaluated the effect of the human immunodeficiency virus (HIV) protease inhibitor saquinavir on the imatinib-sensitive and imatinib-resistant chronic myelogenous leukemia cell lines. Saquinavir, which is also a proteasome blocker, showed dose- and time-related anti-proliferative activity, particularly on the imatinib-resistant lines and a pro-apoptotic effect. Association with imatinib caused a significant increase of activity.
IT 152459-95-5, Imatinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(saquinavir inhibited proliferation and promoted apoptosis in imatinib-resistant chronic myelogenous leukemia cell lines)
RN 152459-95-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

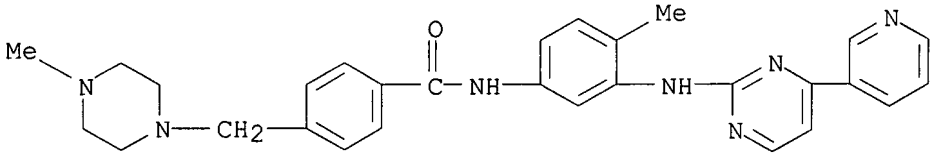
L17 ANSWER 35 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:504246 CAPLUS
DN 146:274241
TI Imatinib mesylate - synthesis methods and preparation of polymorphs
AU Szczepek, Wojciech J.
CS Inst. Farm., Warsaw, 01-793, Pol.
SO Przemysl Chemiczny (2006), 85(5), 306-309
CODEN: PRCHAB; ISSN: 0033-2496
PB Wydawnictwo SIGMA-NOT
DT Journal; General Review
LA Polish
AB A review covering syntheses of 4-(4-methylpiperazin-1-ylmethyl)-N-{4-methyl-3-[4-(pyridin-3-yl)pyrimidyn-2-ylamino]phenyl}benzamide (imatinib) and its polymorphism, preparation of salt adducts, and particularly the 6-step synthesis of imatinib mesylate and its α-polymorph as developed at the Pharmaceutical Research Inst. (Warsaw).
IT 152459-95-5P, Imatinib 220127-57-1P, Imatinib mesylate
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation and polymorphism of)
RN 152459-95-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

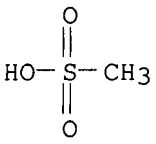
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



L17 ANSWER 36 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:496044 CAPLUS
DN 144:495400
TI Polymorphic forms of imatinib mesylate
IN Kompella, Amala Kishan; Rao, Adibhatla Kali Satya Bhujanga; Podili, Khadgapathi; Chowdary, Nannapaneni Venkaiah
PA Natco Pharma Limited, India
SO PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006054314	A1	20060526	WO 2005-IN273	20050811
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	IN 2004CH01206	A	20061110	IN 2004-CH1206	20041117
PRAI	IN 2004-CH1206	A	20041117		

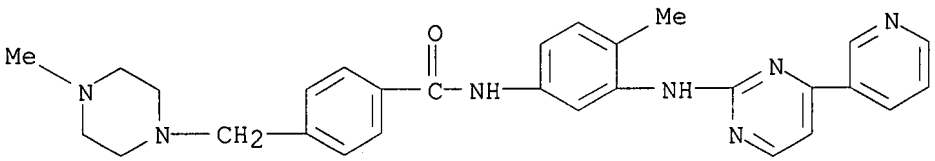
AB The present invention relates to novel crystalline polymorphic Form I & Form II of imatinib mesylate and methods for their preparation The Form I is prepared by slurrying imatinib mesylate α2 or β polymorphic Form in chloroform and water with heating and distilling off water followed by filtration. Form II is prepared by lyophilizing an aqueous solution of polymorph α2 or β. The invention also relates to pharmaceutical composition containing the new Forms useful for the treatment of chronic myelogenous leukemia and accelerated stress conditions for the treatment of chronic myelogenous leukemia and accelerated stress conditions.

IT 220127-57-1P, Imatinib mesylate
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(polymorphic forms of imatinib mesylate)

RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

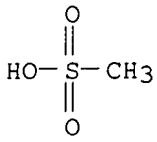
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O

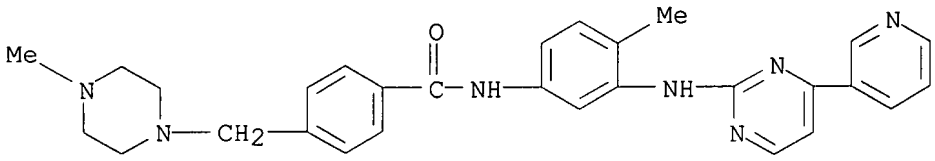


CM 2

CRN 75-75-2
CMF C H4 O3 S



IT 152459-95-5, Imatinib
RL: RCT (Reactant); RACT (Reactant or reagent)
(polymorphic forms of imatinib mesylate)
RN 152459-95-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

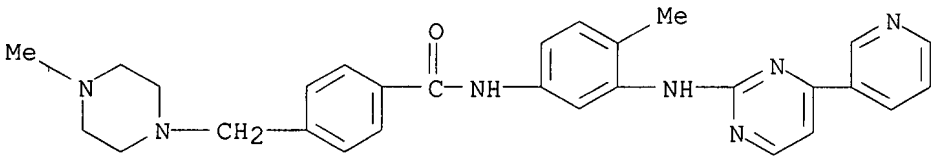
L17 ANSWER 37 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:439489 CAPLUS
DN 144:450736
TI Process for the preparation of a polymorphic crystalline form of imatinib mesylate
IN Patel, Hetalkumar Virendrabhai; Jani, Raja Jyotir; Thennati, Rajamannar
PA Sun Pharmaceutical Industries Limited, India
SO PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006048890	A1	20060511	WO 2005-IN340	20051020
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
IN 2004MU01188	A	20060609	IN 2004-MU1188	20041104
PRAI IN 2004-MU1188	A	20041104		

AB A method for the preparation of a polymorphic crystalline form of imatinib mesylate in a non-needle shaped α-crystalline form is presented. This crystalline form of imatinib mesylate is characterized in that the difference between the tapped and untapped d. is <0.15 g/mL.
IT 220127-57-1, Imatinib mesylate
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); PROC (Process)
(process for the preparation of a polymorphic crystalline form of imatinib mesylate)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

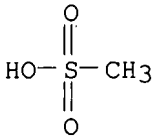
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

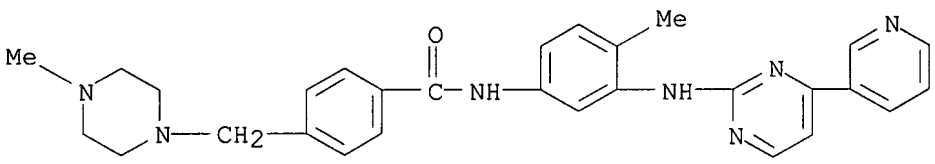
L17 ANSWER 38 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:367158 CAPLUS
DN 144:398362
TI Controlled-release gastric floating matrix formulation containing Imatinib
IN Parvataneni, Durga Maheswari; Rongala, Appala Swamy Naidu; Podile, Khadgapathi; Venkaiah Chowdary, Nannapaneni
PA Natco Pharma Limited, India
SO PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006040779	A2	20060420	WO 2005-IN333	20051006
	WO 2006040779	A3	20060817		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	IN 2004CH01049	A	20070216	IN 2004-CH1049	20041011
PRAI	IN 2004-CH1049	A	20041011		

AB A pharmaceutical formulation and a process for the preparation of controlled release gastric floating matrix solid oral dosage form of Imatinib or its pharmaceutically acceptable salts and its polymorphs such as β, α2, Form I and Form 2 thereof for once daily administration in the form of coated tablet or minitablets and/or pellets filled in hard gelatin capsules are disclosed.

IT 152459-95-5, Imatinib 220127-57-1, Imatinib mesylate
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(controlled-release gastric floating matrix formulation containing Imatinib)

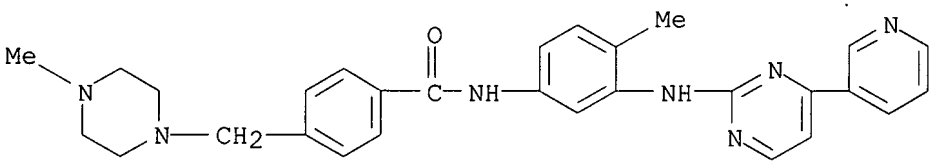
RN 152459-95-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

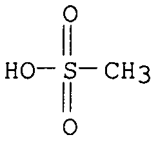
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O

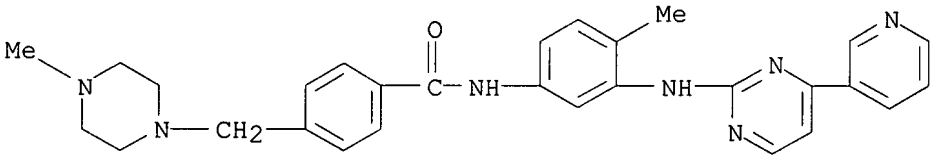


CM 2

CRN 75-75-2
CMF C H4 O3 S



L17 ANSWER 39 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:312180 CAPLUS
DN 145:306234
TI Influence of coagulation factor, vitamin K epoxide reductase complex subunit 1, and cytochrome P450 2C9 gene polymorphisms on warfarin dose requirements
AU Aquilante, Christina L.; Langaee, Taimour Y.; Lopez, Larry M.; Yarandi, Hossein N.; Tromberg, Jennifer S.; Mohuczy, Dagmara; Gaston, Katherine L.; Waddell, Cassandra D.; Chirico, Mark J.; Johnson, Julie A.
CS Department of Pharmacy Practice, Malcolm Randall Veterans Administration Medical Center, University of Florida College of Pharmacy, Gainesville, FL, USA
SO Clinical Pharmacology & Therapeutics (New York, NY, United States) (2006), 79(4), 291-302
CODEN: CLPTAT; ISSN: 0009-9236
PB Elsevier
DT Journal
LA English
AB Introduction: The primary objective of this study was to determine whether variability in warfarin dose requirements is determined by common polymorphisms in genes whose products are involved in the pharmacodynamics and pharmacokinetics of warfarin, namely, the coagulation factors, vitamin K epoxide reductase complex subunit 1 (VKORC1), and cytochrome P 450 (CYP) 2C9. Methods: Patients (N = 350) receiving stable doses of warfarin at 3 consecutive visits were enrolled, and a DNA sample was collected. Samples were genotyped for polymorphisms in the factor II, factor VII, factor X, VKORC1, and CYP2C9 genes. A stepwise linear regression anal. was used to determine the independent effects of genetic and nongenetic factors on mean warfarin dose requirements. Results: Variables associated with lower warfarin dose requirements were VKORC1 3673 AA genotype ($P < .0001$), VKORC1 3673 GA genotype ($P < .0001$), 1 variant CYP2C9 allele ($P < .0001$), 2 variant CYP2C9 alleles ($P = .0004$), increasing age ($P = .0005$), concomitant CYP2C9 inhibitors ($P = .0005$), and goal international normalized ratio ($P = .01$). Variables associated with higher warfarin dose requirements were weight ($P < .0001$), current smoker status ($P = .0009$), mean international normalized ratio ($P = .001$), concomitant CYP2C9 inducers ($P = .006$), factor X insertion/deletion genotype ($P = .01$), factor X insertion/insertion genotype ($P = .04$), factor VII deletion/deletion genotype ($P = .04$), and calculated vitamin K intake ($P = .05$). The linear regression model explained 51.4% of the variability in warfarin dose requirements. Conclusion: Polymorphisms in warfarin drug target and metabolizing enzyme genes, in addition to nongenetic factors, were important determinants of warfarin dose requirements.
IT 152459-95-5, Imatinib
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cytochrome P 450 2C9 inhibitor imatinib was associated with low warfarin dose requirement in patient undergoing stable warfarin anticoagulant therapy)
RN 152459-95-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)

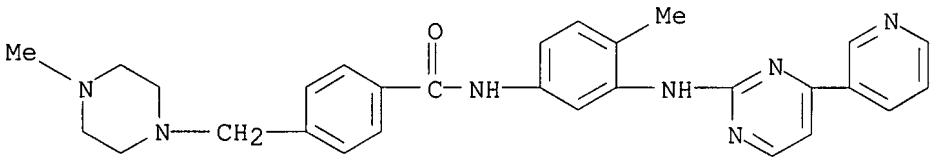


RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 40 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:229169 CAPLUS
DN 144:403621
TI Functional SNPs of the breast cancer resistance protein - therapeutic effects and inhibitor development
AU Yanase, Kae; Tsukahara, Satomi; Mitsuhashi, Junko; Sugimoto, Yoshikazu
CS Department of Chemotherapy, Kyoritsu University of Pharmacy, 1-5-30 Shibakoen, Minato-ku, Tokyo, 105-8512, Japan
SO Cancer Letters (Amsterdam, Netherlands) (2006), 234(1), 73-80
CODEN: CALEDQ; ISSN: 0304-3835
PB Elsevier B.V.
DT Journal; General Review
LA English
AB A review. Breast cancer resistance protein (BCRP) is a half-mol. ATP-binding cassette transporter that pumps out various anticancer agents such as 7-ethyl-10-hydroxycamptothecin, topotecan, and mitoxantrone. We have previously identified three polymorphisms within the BCRP gene, G34A (substituting Met for Val-12), C376T (substituting a stop codon for Gln-126), and C421A (substituting Lys for Gln-141). C421A BCRP-transfected murine fibroblast PA317 cells showed markedly decreased protein expression and low-level drug resistance when compared with wild-type BCRP-transfected cells. In contrast, G34A BCRP-transfected PA317 cells showed a similar protein expression and drug resistance profile to wild-type. The C376T polymorphism would be expected to have a considerable impact as active BCRP protein will not be expressed from a T376 allele. Hence, people with C376T and/or C421A polymorphisms may express low levels of BCRP, resulting in hypersensitivity of normal cells to BCRP-substrate anticancer agents. Estrogens, estrone, and 17β-estradiol were previously found to restore drug sensitivity levels in BCRP-transduced cells by increasing the cellular accumulation of anticancer agents. BCRP transports sulfated estrogens but not free estrogens and in a series of screening expts. for synthesized and natural estrogenic compds., several tamoxifen derivs. and phytoestrogens/flavonoids were identified that effectively circumvent BCRP-mediated drug resistance. The kinase inhibitors gefitinib and imatinib mesylate also interact with BCRP. Gefitinib, an inhibitor of epidermal growth factor receptor-tyrosine kinase, inhibits its transporter function and reverses BCRP-mediated drug resistance both in vitro and in vivo. BCRP-transfected human epidermoid carcinoma A431 cells and BCRP-transfected human non-small cell lung cancer PC-9 cells show gefitinib resistance. Imatinib, an inhibitor of BCR-ABL tyrosine kinase, also inhibits BCRP-mediated drug transport. Hence, both functional SNPs and inhibitors of BCRP reduce its transporter function and thus modulate substrate pharmacokinetics and pharmacodynamics.
IT 220127-57-1, Imatinib mesylate
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic effects and inhibitor development for functional SNPs of breast cancer resistance protein)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

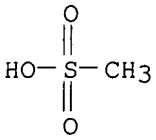
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S

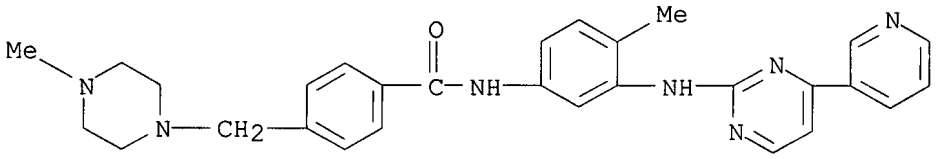


RE.CNT 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 41 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:211340 CAPLUS
DN 145:159216
TI The role of the K247R substitution in the ABL tyrosine kinase domain in sensitivity to imatinib
AU Nicolini, Franck Emmanuel; Chabane, Kaddour; Cayuela, Jean-Michel; Rousselot, Philippe; Thomas, Xavier; Hayette, Sandrine
CS Hematology Department, Hopital Ed. Herriot, Lyon, Fr.
SO Haematologica (2006), 91(1), 137-138
CODEN: HAEMAX; ISSN: 0390-6078
PB Ferrata Storti Foundation
DT Journal
LA English
AB Imatinib mesylate has become the gold standard front-line treatment of chronic myelogenous leukemia through its ability to inhibit ABL tyrosine kinase. Resistance to this inhibition may occur. We investigated the role of the K247R polymorphism in persistent sensitivity.
IT 220127-57-1, Imatinib mesylate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ABL tyrosine kinase gene K247R polymorphism associated with F317L mutation had no impact on persistent sensitivity to imatinib mesylate in chronic myelogenous leukemia patient)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

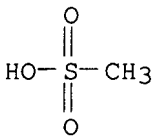
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S

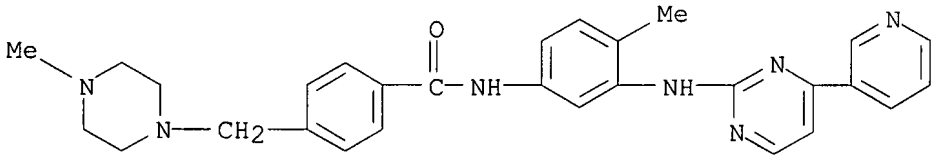


RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 42 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:183686 CAPLUS
DN 144:305016
TI Mutation and expression of PDGFRA and KIT in malignant peripheral nerve sheath tumors, and its implications for imatinib sensitivity
AU Holtkamp, Nikola; Okuducu, Ali Fuat; Mucha, Jana; Afanasieva, Anastasia; Hartmann, Christian; Atallah, Isis; Estevez-Schwarz, Lope; Mawrin, Christian; Friedrich, Reinhard E.; Mautner, Victor-F.; von Deimling, Andreas
CS Institute of Neuropathology, Charite-Universitaetsmedizin Berlin, Germany
SO Carcinogenesis (2006), 27(3), 664-671
CODEN: CRNGDP; ISSN: 0143-3334
PB Oxford University Press
DT Journal
LA English
AB Platelet-derived growth factor receptor alpha (PDGFRα) and c-Kit are receptor tyrosine kinases. Both are targets of the tyrosine kinase inhibitor imatinib mesylate which is approved for treatment of some cancers. To assess the role of PDGFRα and c-Kit in malignant peripheral nerve sheath tumors (MPNST) we examined human tumors for structural alterations, protein and ligand expression. We investigated 34 MPNST, 6 corresponding plexiform neurofibromas (pNF) and 1 MPNST cell culture from 31 patients for mutations and polymorphisms in PDGFRA (exon 2-21) and KIT (exon 9, 11, 13, 17). PDGFRA was amplified in seven tumors from six patients and MPNST cell culture S462. KIT was amplified in five tumors from four patients and in the cell culture. Two MPNST carried somatic PDGFRA mutations in exons coding for the extracellular domain. In addition we detected several polymorphisms in PDGFRA. No point mutations or polymorphisms were detected in the four KIT exons analyzed. PDGFRα expression was present in 21 of 28 MPNST patients (75%) and the MPNST cell culture. Expression anal. of PDGFRα ligands in MPNST and neurofibromas revealed that PDGF-A was more widely expressed than PDGF-B. Focal c-Kit expression was detected in 2 of 29 (7%) MPNST patients. Imatinib treatment of MPNST cell culture S462 exerted a growth inhibitory effect and prevented PDGF-AA induced PDGFRα phosphorylation. In summary, PDGFRA, PDGF and KIT dysregulation as well as growth inhibition of cell culture S462 by imatinib may suggest that MPNST patients benefit from treatment with imatinib.
IT 220127-57-1, Imatinib mesylate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mutation and expression of PDGFRα and c-KIT in malignant peripheral nerve sheath tumors, and its implications for imatinib sensitivity)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

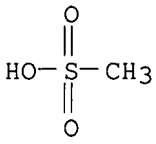
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 43 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:167588 CAPLUS
DN 144:254148
TI Aminopteridinones as anticancer agents, their preparation, pharmaceutical compositions, and use in therapy
IN Munzert, Gerd; Steegmaier, Martin; Baum, Anke
PA Boehringer Ingelheim International G.m.b.H., Germany; Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G.
SO PCT Int. Appl., 158 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006018182	A1	20060223	WO 2005-EP8623	20050809
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	US 2006058311	A1	20060316	US 2005-189540	20050726
	AU 2005274384	A1	20060223	AU 2005-274384	20050809
	CA 2576269	A1	20060223	CA 2005-2576269	20050809
	EP 1827441	A1	20070905	EP 2005-770228	20050809
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BA, HR, YU				
	IN 2007DN00888	A	20070803	IN 2007-DN888	20070202
PRAI	EP 2004-19361	A	20040814		
	EP 2004-19448	A	20040817		
	WO 2005-EP8623	W	20050809		

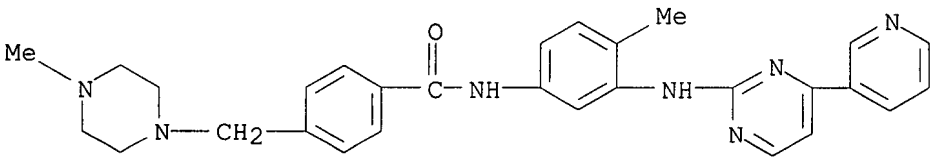
OS MARPAT 144:254148
AB The invention relates to a group of aminopteridinones I, which are useful for the treatment of diseases which involve cell proliferation. In compds. I, R1 and R2 are independently selected from H and (un)substituted C1-6 alkyl, or R1 and R2 together form a 2- to 5-membered alkylene bridge, optionally containing 1 or 2 heteroatoms; R3 is (un)substituted C1-12 alkyl, C2-12 alkenyl, C2-12 alkynyl, C6-14 aryl, etc.; R4 is H, OH, CN, halo, (un)substituted amino, (un)substituted C1-6 alkyl, C1-5 alkoxy, etc.; L is (un)substituted C2-10 alkylene, (un)substituted C2-10 alkenylene, (un)substituted C6-14 arylene, etc.; R5 is (un)substituted morpholinyl, (un)substituted piperidinyl, (un)substituted piperazinyl, (un)substituted piperazinylcarbonyl, (un)substituted pyrrolidinyl, (un)substituted thiomorpholinyl, etc.; n is 0 or 1; and m is 1 or 2; including tautomers, stereoisomers, salts, solvates, polymorphs, and prodrugs thereof. The invention also relates to the preparation of I, pharmaceutical compns. comprising a compound I, at least one other therapeutic agent, optionally with one or more pharmaceutically acceptable excipients, as well as to the use of the compns. for the treatment of diseases which involve cell proliferation, migration or apoptosis of cancer cells, or angiogenesis. Esterification of (R)-2-aminobutyric acid and reductive condensation with cyclopentanone gave cyclopentylamine II, which underwent

regioselective substitution of 2,4-dichloro-5-nitropyrimidine and reductive heterocyclization to form pteridinone III. N-Methylation of III followed by substitution with 4-amino-3-methoxybenzoic acid and amidation with 1-methyl-4-aminopiperidine resulted in the formation of aminopteridinone IV. A combination of suboptimal doses of irinotecan and compound IV shows an additive/synergistic effect in a human colon carcinoma model and is well tolerated. Meanwhile, compound IV acts at least additively with docetaxel in a human non-small cell lung carcinoma model and not antagonistically with gemcitabine in a human adenocarcinoma model.

IT 152459-95-5, Imatinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of aminopteridinones for use in combination therapy for treatment of cell proliferative diseases)

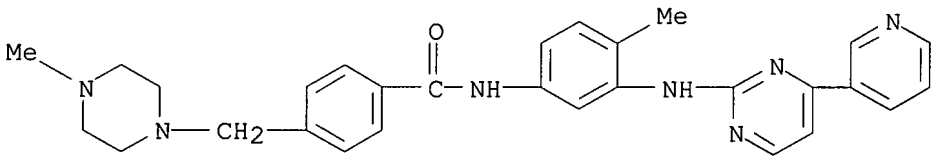
RN 152459-95-5 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 44 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:1140722 CAPLUS
DN 144:205280
TI A single nucleotide polymorphism in the coding region of ABL and its effects on sensitivity to imatinib
AU Crossman, L. C.; O'Hare, T.; Lange, T.; Willis, S. G.; Stoffregen, E. P.; Corbin, A. S.; O'Brien, S. G.; Heinrich, M. C.; Druker, B. J.; Middleton, P. G.; Deininger, M. W. N.
CS Oregon Health & Science University Cancer Institute, Portland, OR, USA
SO Leukemia (2005), 19(11), 1859-1862
CODEN: LEUKED; ISSN: 0887-6924
PB Nature Publishing Group
DT Journal
LA English
AB We have identified a gene polymorphism (K247R) within or close to the P-loop of BCR-ABL, which leads to the substitution of arginine for lysine. We investigated the allelic frequency of K247R by screening 157 CML patients and 213 healthy blood donors with conventional sequencing, restriction enzyme digest and single strand conformational polymorphism anal., and found the arginine allele to be rare. Three out of five CML patients with the arginine allele of K247R failed to achieve a major cytogenetic response to imatinib, suggesting that the arginine allele may have reduced sensitivity. However, despite K247R's position in or near to the P-loop, biochem. and cellular assays of imatinib and dasatinib sensitivity showed no alteration compared to wild type. Clinicians should be aware that possession of the arginine allele of K247R does not reflect a mutation that necessitates a change in the therapeutic strategy, unless there are other signs of inadequate response to drug.
IT 152459-95-5, Imatinib
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(single nucleotide polymorphism K247R in coding region of BCR-ABL gene with arginine allele for lysine failed to achieve major cytogenetic response to imatinib indicating arginine may reduce sensitivity to imatinib in CML patient)
RN 152459-95-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 45 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:1106857 CAPLUS
DN 143:392946
TI Preparation of crystalline methanesulfonic acid addition salts of imatinib
IN Szczepek, Wojciech; Samson-Lazinska, Dorota; Zagrodzki, Bogdan; Glice, Magdalena; Maruszak, Wioleta; Korczak, Kataryzna; Modzelewski, Ryszard; Lawecka, Marta; Kaczmarek, Lukasz; Szelejewski, Wieslaw; Fraczek, Urszula; Cmoch, Piotr
PA Instytut Farmaceutyczny, Pol.
SO PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

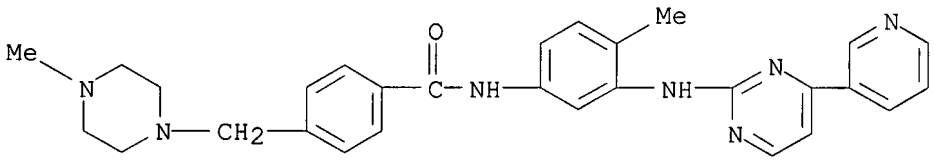
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005095379	A2	20051013	WO 2005-PL24	20050402
	WO 2005095379	A3	20060518		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1742933	A2	20070117	EP 2005-731354	20050402
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU				
	US 2007197545	A1	20070823	US 2006-599461	20060929
PRAI	PL 2004-366885	A	20040402		
	PL 2005-374074	A	20050401		
	WO 2005-PL24	W	20050402		

AB The invention relates to the methanesulfonic acid addition salts of imatinib and to the processes for their preparation In particular, the invention relates to the process for the preparation of imatinib methanesulfonate α-crystal form. Furthermore, the invention is directed to a novel acid addition salt of imatinib with 2 mols. of methanesulfonic acid and the polymorphic forms thereof as well as their pharmaceutical compns. The suspension of imatinib in anhydrous EtOH was heated to 75°, and methanesulfonic acid was slowly added dropwise. EtOAc was added and the mixture was cooled to 30°, while being stirred. The seeds of α-crystal form were added and then the mixture was cooled and stirred at 13-20° for 4 h. The crystals were filtered off, and dried to obtain α-crystal form of imatinib mesylate yield: 65.0%.
IT 866527-60-8P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation of crystalline methanesulfonic acid addition salts of imatinib)
RN 866527-60-8 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, dimethanesulfonate (9CI) (CA INDEX NAME)

CM 1

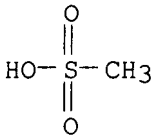
CRN 152459-95-5

CMF C29 H31 N7 O



CM 2

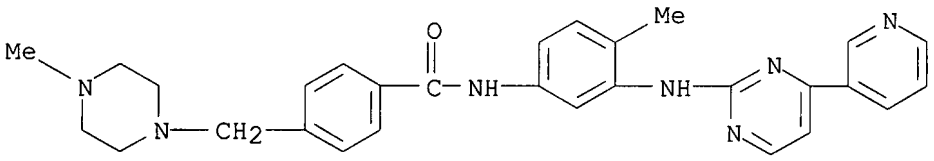
CRN 75-75-2
CMF C H4 O3 S



IT 220127-57-1P, IMatinib mesylate
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of crystalline methanesulfonic acid addition salts of imatinib)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

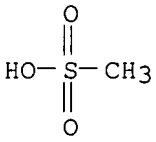
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O

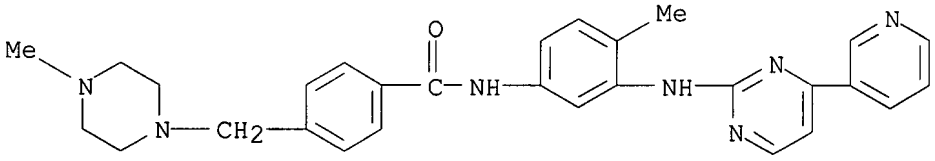


CM 2

CRN 75-75-2
CMF C H4 O3 S



IT 152459-95-5, Imatinib
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(preparation of crystalline methanesulfonic acid addition salts of imatinib).
RN 152459-95-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



L17 ANSWER 46 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:1026883 CAPLUS
DN 143:324151
TI Protein tyrosine phosphatase PTPN22 polymorphisms in diagnosis and therapy of rheumatoid arthritis and related disorders
IN Broder, Samuel E.; Booth, Robert F.
PA Celera, An Applera Corporation Business, USA
SO PCT Int. Appl., 140 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005086872	A2	20050922	WO 2005-US7800	20050308
WO 2005086872	A3	20060309		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2004-552216P P 20040310

AB This invention relates to the discovery that polymorphisms of the intracellular tyrosine phosphatase PTPN22 are associated with cellular proliferative, immune system, and inflammatory disorders in humans. Over 12,000 SNPs from throughout the entire genome were screened in the discovery sample set cohort which lead to the discovery that polymorphisms of the PTPN22 are statistically associated with the occurrence of rheumatoid arthritis in humans. SNP-1 represents a missense mutation at position 1970 of the transcript DNA wherein the nucleotide residue is a T rather than a C, and the polymorphism encodes a tryptophan rather than an arginine in PTPN22 protein at position 620. The SNP-1 polymorphism occurs much more often (about 15%) in a population having rheumatoid arthritis as compared to a control population. The odds ratio is about 1.7 and indicates that the SNP-1 polymorphism occurs nearly twice as frequently in patients with rheumatoid arthritis than in well-matched controls. The invention provides: (1) methods and compns. for detecting polymorphisms of the PTPN22 genomic DNA; (2) methods for associating polymorphisms of the PTPN22 gene with the occurrence of an immune disorder, inflammatory disorder or cell proliferation disorder; (3) methods for identifying subjects at risk of an immune disorder, inflammatory disorder or cell proliferation disorder by determining if they have a polymorphism of the PTPN22 gene and treating such subjects with a tyrosine kinase inhibitor to prevent or delay the progression of such diseases; (4) methods for identifying subjects having an immune disorder, inflammatory disorder or cell proliferation disorder who are promising candidates for therapy with a tyrosine kinase inhibitor by determining if such subjects have a polymorphism of the PTPN22 gene; and (5) methods of treating subjects having an immune disorder, inflammatory disorder or cell proliferation disorder mediated by a polymorphism of the PTPN22 gene by administering to such subjects a tyrosine kinase inhibitor.

IT 220127-57-1, Imatinib mesylate
RL: BSU (Biological study, unclassified); BIOL (Biological study)

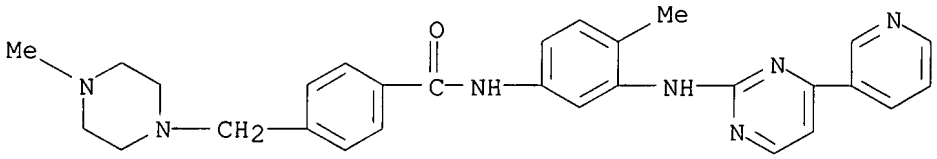
(protein tyrosine phosphatase PTPN22 polymorphisms in diagnosis and therapy of rheumatoid arthritis and related disorders)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

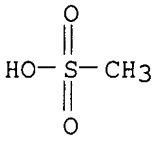
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



L17 ANSWER 47 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:902882 CAPLUS
DN 143:235468
TI Novel polymorphic form of imatinib mesylate and a process for its preparation
IN Amala, Kompella; Srinivasa Rao, Thungathurthi; Adibhatla Kali Satya, Bhujanga Rao; Rachakonda, Sreenivas; Venkaiah Chowdary, Nannapaneni; Podili, Khadgapathi
PA Natco Pharma Limited, India
SO PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

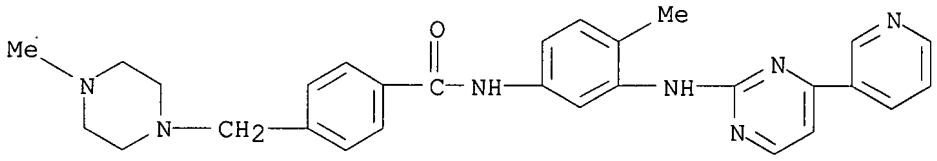
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005077933	A1	20050825	WO 2004-IN352	20041116
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IN 2004CH00105	A	20070302	IN 2004-CH105	20040211
IN 2004CH00706	A	20060623	IN 2004-CH706	20040720
IN 2004CH00712	A	20070914	IN 2004-CH712	20040721
CA 2555804	A1	20050825	CA 2004-2555804	20041116
EP 1720853	A1	20061115	EP 2004-806748	20041116
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
PRAI IN 2004-CH105	A	20040211		
WO 2004-IN352	W	20041116		

AB This invention discloses a novel stable crystal form of imatinib mesylate, designated by us as α2 Form, which is stable at room temperature and even at higher temps. up to 120 °C and accelerated stress conditions and, freely soluble in water. This invention also discloses a pharmaceutical composition containing the novel stable α2 form of Imatinib mesylate and other usually employed excipients, useful in the treatment of Chronic Myelogenous Leukemia (CML). This new α2 Form of imatinib mesylate is prepared by slurrying Imatinib base in isopropanol at room temperature followed by addition of methane sulfonic acid and maintaining 50-60 °C followed by filtration. This invention also discloses another process for the preparation of the novel, stable α2 crystalline form of Imatinib Mesylate by the conversion of Imatinib mesylate β- polymorphic modification by suspending it in water and organic solvents, distilling off water azeotropically, cooling and filtering to obtain the α2 crystal form.
IT 220127-57-1P, Imatinib mesylate
RL: IMF (Industrial manufacture); PEP (Physical, engineering or chemical process); PNU (Preparation, unclassified); PRP (Properties); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(novel polymorphic form of imatinib mesylate and a process for its preparation)

RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

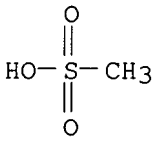
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O

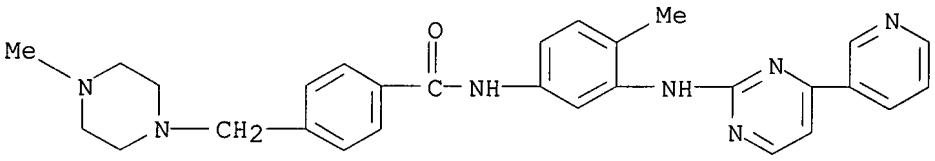


CM 2

CRN 75-75-2
CMF C H4 O3 S



IT 152459-95-5, Imatinib
RL: RCT (Reactant); RACT (Reactant or reagent)
(novel polymorphic form of imatinib mesylate and a process for its preparation)
RN 152459-95-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)

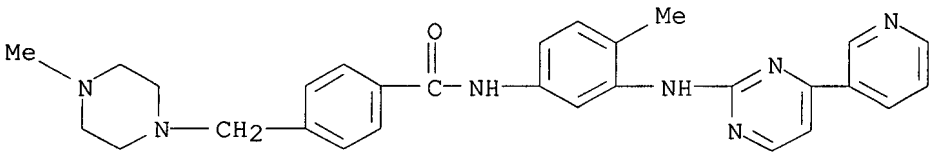


RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 48 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:404225 CAPLUS
DN 143:109151
TI Effects of STI571 (gleevec) on pancreatic cancer cell growth
AU Li, Junsheng; Kleeff, Joerg; Guo, Junchao; Fischer, Lars; Giese, Nathalia; Buechler, Markus W.; Friess, Helmut
CS Department of General Surgery, University of Heidelberg, Heidelberg, 69120, Germany
SO Molecular Cancer (2003), 2, No pp. given
CODEN: MCOACG; ISSN: 1476-4598
URL: http://www.molecular-cancer.com/content/pdf/1476-4598-2-32.pdf
PB BioMed Central Ltd.
DT Journal; (online computer file)
LA English
AB Background: Pancreatic cancer is an aggressive malignancy characterized by low responsiveness to chemotherapy and radiotherapy. This resistance is partly due to the overexpression of several tyrosine kinase receptors and their ligands. STI571 has specific activity in inhibiting c-kit, PDGF and Abl receptor tyrosine kinases and has proven successful in the treatment of CML and GIST patients. Here, we investigated the potential role of STI571 in pancreatic cancer. Results: The GI50 of STI571 as well as the effects of STI571 on growth factor actions in pancreatic cell lines were analyzed using the MTT assay. FACS anal. using Annexin and PI staining was performed to study cell cycle, apoptosis, and cell death. Western blot anal. was carried out to investigate MAP kinase and receptor tyrosine kinase phosphorylation. STI571 inhibited cell proliferation in pancreatic cancer cell lines with GI50 concns. ranging from 17 to 31.5 microM. EGF, IGF-1, and FGF-2 but not PDGF exerted growth stimulatory effects in pancreatic cancer cell lines. STI571 only partly blocked these effects on cell growth, and did not abrogate growth factor-induced receptor and MAPK phosphorylation. Conclusion: Our data demonstrate that STI571 inhibits pancreatic cancer cell growth with high GI50 concns. through tyrosine-kinase receptor independent pathways. The clin. application of STI571 in pancreatic cancer is therefore rather doubtful.
IT 220127-57-1, Gleevec
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(C1744T transition is common polymorphism which result in Pro582Ser change in ODD domain of HIF-1α does not impair either Pro-564 hydroxylation or its subsequent recognition by VHL protein in patient with idiopathic erythrocytosis)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

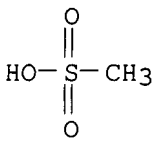
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S

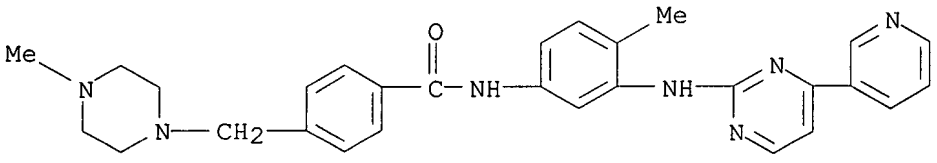


RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 49 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:312458 CAPLUS
DN 143:42398
TI Characteristic of two mouse bcr-abl-transformed cell lines: I. General properties of the cells
AU Sobotkova, E.; Ludvikova, V.; Petrackova, M.; Duskova, M.; Smetana, K.; Jelinek, F.; Marinov, I.; Vonka, V.
CS Department of Experimental Virology, Institute of Hematology and Blood Transfusion, Prague, Czech Rep.
SO Folia Biologica (Prague, Czech Republic) (2005), 51(1), 12-18
CODEN: FOBLAN; ISSN: 0015-5500
PB Institute of Molecular Genetics
DT Journal
LA English
AB In an effort to develop an exptl. system suitable for immunol. studies in which Bcr-Abl-pos. cells are to be used as antigens, we examined the properties of two mouse (Balb/c) established cell lines that express the Bcr-Abl protein and are oncogenic for syngeneic animals. Under standard conditions the two cell lines, viz. Ba-p210 (B210) and 12B1, expressed comparable amts. of the Bcr-Abl protein. However, they differed in a number of characteristics. From the morphol. point of view, B210 cells were the more homogeneous, being mainly represented by leukemic blastic cells with a large number of AgNORs as markers indicating a high proliferative activity. 12B1 cells were more polymorphic and giant cells were detected within their populations. Many 12B1 cells exhibited nuclear segmentation and "band-like" structures. Markers of proliferation were less frequent in 12B1 and the tendency for aging was more pronounced in these cells. The 12B1 cells were slightly more sensitive to imatinib mesylate than B210 cells. In B210 cells, the expression of MHC class I was down-regulated, which was not the case with 12B1 cells. Both cell lines induced leukemia-like disease in mice after i.v. application but, as compared with B210, 12B1 cells were about 100 times more oncogenic and the disease they induced was more aggressive. Moreover, 12B1, but not B210, induced tumors after s.c. or i.p. inoculation.
IT 220127-57-1, Imatinib mesylate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oncogenic activities of mouse bcr-abl transformed cell lines and sensitivity to)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

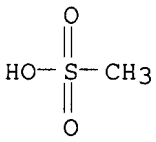
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S

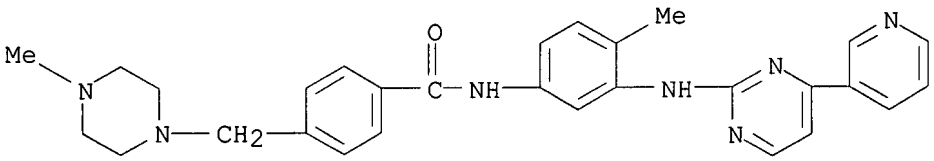


RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 50 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:307632 CAPLUS
DN 142:441150
TI Pharmacogenomics and the drug discovery pipeline: when should it be implemented?
AU Penny, Michelle A.; McHale, Duncan
CS Clinical Pharmacogenomics, Pfizer Global Research and Development, Sandwich, UK
SO American Journal of PharmacoGenomics (2005), 5(1), 53-62
CODEN: AJPMC8; ISSN: 1175-2203
PB Adis International Ltd.
DT Journal; General Review
LA English
AB A review. One of the key factors in developing improved medicines lies in understanding the mol. basis of the complex diseases we treat. Investigation of genetic assocns. with disease utilizing advances in linkage disequil.-based whole genome association strategies will provide novel targets for therapy and define relevant pathways contributing to disease pathogenesis. Genetic studies in conjunction with gene expression, proteomic, and metabonomic analyses provide a powerful tool to identify mol. subtypes of disease. Using these mol. data, pharmacogenomics has the potential to impact on the drug discovery and development process at many stages of the pipeline, contributing to both target identification and increased confidence in the therapeutic rationale. This is exemplified by the identified association of 5-lipoxygenase-activating protein (ALOX5AP/FLAP) with increased risk of myocardial infarction, and of the chemokine receptor 5 (CCR5) with HIV infection and therapy. Pharmacogenomics has already been used in oncol. to demonstrate that mol. data facilitates assessment of disease heterogeneity, and thus identification of mol. markers of response to drugs such as imatinib mesylate (Gleevec) and trastuzumab (Herceptin). Knowledge of genetic variation in a target allows early assessment of the clin. significance of polymorphism through the appropriate design of preclin. studies and use of relevant animal models. A focused pharmacogenomic strategy at the preclin. phase of drug development will produce data to inform the pharmacogenomic plan for exploratory and full development of compds. Opportunities post-approval show the value of large well-characterized data sets for a systematic assessment of the contribution of genetic determinants to adverse drug reactions and efficacy. The availability of genomic samples in large phase IV trials also provides a valuable resource for further understanding the mol. basis of disease heterogeneity, providing data that feeds back into the drug discovery process in target identification and validation for the next generation of improved medicines.
IT 220127-57-1, Gleevec
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacogenomics could be used for drug discovery pipeline in oncol. for assessment of mol. data facilities of disease heterogeneity and identification of mol. markers in response to imatinib mesylate, trastuzumab drugs)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

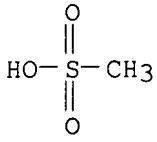
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



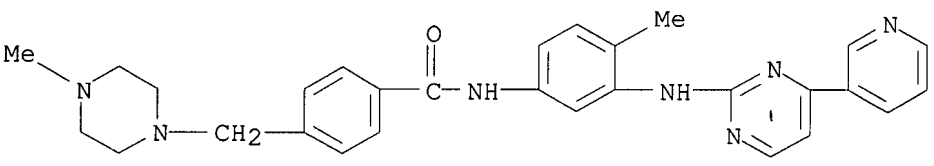
CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 86 THERE ARE 86 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 51 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:149182 CAPLUS
DN 142:456387
TI Imatinib pharmacokinetics in patients with gastrointestinal stromal tumour: a retrospective population pharmacokinetic study over time. EORTC Soft Tissue and Bone Sarcoma Group
AU Judson, Ian; Ma, Peiming; Peng, Bin; Verweij, Jaap; Racine, Amy; Paola, Eugenio Donato; Glabbeke, Martine; Dimitrijevic, Sasa; Scurr, Michelle; Dumez, Herlinde; Oosterom, Allan
CS Royal Marsden Hospital, London, SW3 6JJ, UK
SO Cancer Chemotherapy and Pharmacology (2005), 55(4), 379-386
CODEN: CCPHDZ; ISSN: 0344-5704
PB Springer GmbH
DT Journal
LA English
AB Imatinib pharmacokinetics (PK) may be affected by a number of factors that are related to the disease being treated and to the response of that disease to imatinib. Patients in the phase I and phase II trials conducted by the EORTC in patients with gastrointestinal stromal tumors (GISTs) and other sarcomas had detailed blood sampling for imatinib PK on day 1 and on day 29. Patients with GISTs also had repeat sampling, using a limited sampling strategy, after approx. 12 mo on therapy. This population PK study was carried out to examine what covariates affected imatinib PK in GIST patients and what PK changes occurred over time. In the model producing the best fit, low clearance (CL) correlated with low body weight and high granulocyte count, whereas low Hb correlated with low volume of distribution. For a patient with 77% of the median body weight or with 1.87 times the median granulocyte count, the apparent CL is 6.53 l/h, about 70% of the typical apparent CL of 9.33 l/h; for a patient of 84% of the typical Hb level, the volume of distribution is about 70%. Total white blood cell count correlated closely with granulocyte count and there was a moderate correlation between Hb and albumin (r=0.454). There was a trend towards increased imatinib clearance after chronic exposure over 12 mo. The typical apparent CL increased 33% from day 1. Nevertheless, the approx. 95% confidence interval of the increase of the typical apparent CL was 33±34.6%, which contains zero. It is not yet clear whether this is a significant factor in the amelioration of imatinib toxicity that occurs with time or is related to disease control, and further work is required to confirm this observation.
IT 152459-95-5, Imatinib
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(imatinib pharmacokinetics showed time-dependent increase in apparent clearance in patient with soft tissue sarcoma and gastrointestinal stromal tumor)
RN 152459-95-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 52 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:76317 CAPLUS
DN 142:171154
TI Protein and cDNA sequences of human FOXO3a and methods for modulating ovarian follicular initiation
IN Castrillon, Diego H.; Depinho, Ronald A.
PA Dana-Farber Cancer Institute, USA
SO PCT Int. Appl., 100 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005007687	A1	20050127	WO 2004-US21814	20040707

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2003-486016P P 20030709

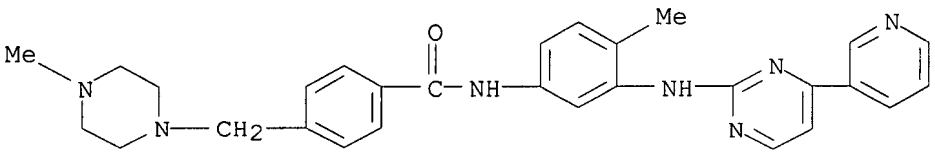
AB The present invention provides methods for modulating ovarian follicular initiation, modulating fertility, treating infertility, and treating hormone-related diseases or disorders comprising modulating the expression or activity of FOXO3a. The present invention provides protein and cDNA sequences of human FOXO3a and identification of single nucleotide polymorphisms in FOXO3a gene, which is indicative of premature ovarian failure in the subject. The present invention also provides an animal, e.g., transgenic mouse, in which the FOXO3a gene is misexpressed. Methods for identifying contraceptive agents are also described. Also described are methods for diagnosing premature ovarian failure (POF).

IT 220127-57-1, Imatinib mesylate
RL: DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(protein and cDNA sequences of human FOXO3a and methods for modulating ovarian follicular initiation)

RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

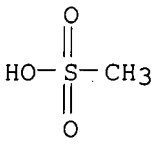
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S

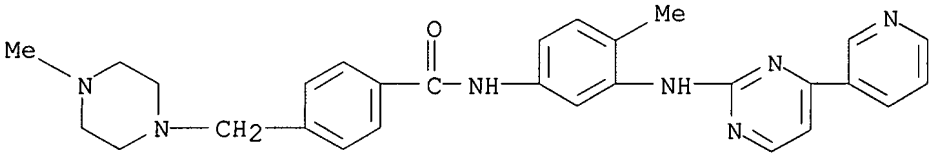


RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 53 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:1047047 CAPLUS
DN 142:253425
TI Anticancer agents and genetic polymorphisms of drug metabolizing enzyme
AU Fujieda, Masaki; Kamataki, Tetsuya
CS Div. of DrugMetabolism, Graduate School of Pharmaceutical Science, Hokkaido University, Japan
SO Jikken Igaku (2004), 22(14), 2061-2065
CODEN: JIIGEF, ISSN: 0288-5514
PB Yodosha
DT Journal; General Review
LA Japanese
AB A review. Anticancer agents and genetic polymorphisms of drug metabolizing enzyme is reviewed including the role of cytochrome P 450, SNP, uridine diphosphate glucuronosyltransferase, and thiopurine methyl-transferase in genetic polymorphisms of antitumor agent metabolizing enzyme with Gleevec, Herceptin, Iressa, and 5-FU etc. as examples.
IT 220127-57-1, Gleevec
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anticancer agents and genetic polymorphisms of drug metabolizing enzyme)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

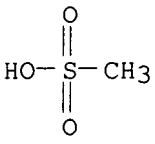
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

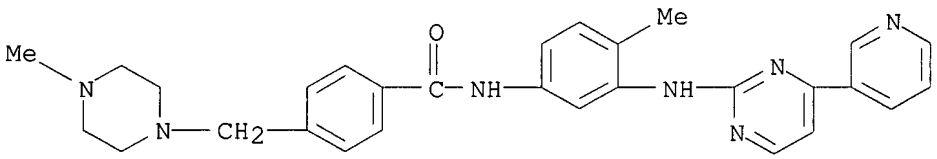
CRN 75-75-2
CMF C H4 O3 S



L17 ANSWER 54 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:836441 CAPLUS
DN 142:170471
TI Application of human genome data to personalized medicine
AU Furukawa, Yoichi; Nakamura, Yusuke
CS Institute of Medical Science, University of Tokyo, Japan
SO BIO Clinica (2004), 19(11), 878-882
CODEN: BCILCY; ISSN: 0919-8237
PB Hokuryukan
DT Journal; General Review
LA Japanese
AB A review discussed the importance of the establishment of genomics information for human individuals in the personalized medication system. The predicting the genetic susceptibility of human individuals to various common and complex diseases by the SNP typing and the comprehensive organization of the genetic information into the database were discussed. Revealing the gene expression patterns in cancers was described as another pathway of the genomics to clin. medicine. Variations of the cancer therapy prognosis dependent on the individual genetic background expecially regarding drug metabolism related to anticancer drug sensitivity and the onset of adversed actions were described with the examples of gleevec-therapy or iressa-therapy.
IT 220127-57-1, Gleevec
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(genetic variation of efficiency of; application of human genome data to personalized medicine)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

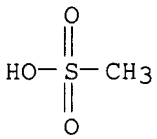
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

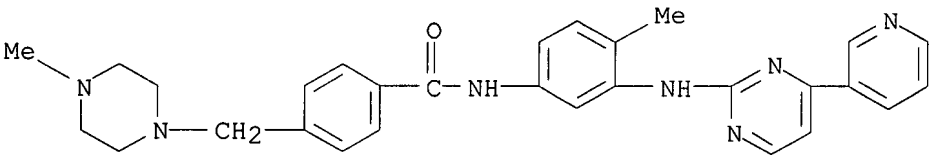
CRN 75-75-2
CMF C H4 O3 S



L17 ANSWER 55 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:776365 CAPLUS
DN 141:405777
TI Development of hygromas or severe edema during treatment with the tyrosine kinase inhibitor STI571 is not associated with platelet-derived growth factor receptor (PDGFR) gene polymorphisms
AU Bruck, Patrick; Wassmann, Barbara; Lopez, Elizabeth Ramos; Hoelzer, Dieter; Ottmann, Oliver G.
CS Department of Hematology and Oncology, Medizinische Klinik III, Johann Wolfgang Goethe-University, Frankfurt, 60590, Germany
SO Leukemia Research (2004), 28(11), 1153-1157
CODEN: LEREDD; ISSN: 0145-2126
PB Elsevier B.V.
DT Journal
LA English
AB STI571 is active against Bcr/Abl-, c-kit- and platelet-derived growth factor receptor (PDGFR)-driven malignancies. Mild to moderate edema is common, whereas severe edema, body cavity effusions and subdural hygromas are rarely observed These effects have been suggested to involve inhibition of PDGFR signaling, but predisposing factors are unknown. We examined SNPs in the PDGFR α and β gene regions in STI571-treated patients with and without life-threatening edema or cerebral hygromas, and in healthy volunteers. By RFLP anal. of 15 SNPs, the frequencies of genotypes did not differ between the three groups. SNPs of PDGFR genes do not appear to play a role in patient's susceptibility to clin. severe edema formation during treatment with STI571.
IT 220127-57-1, STI571
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(STI571 induced hygromas or edema not associated with platelet-derived growth factor receptor gene polymorphisms)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

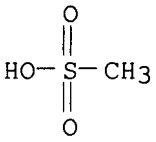
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



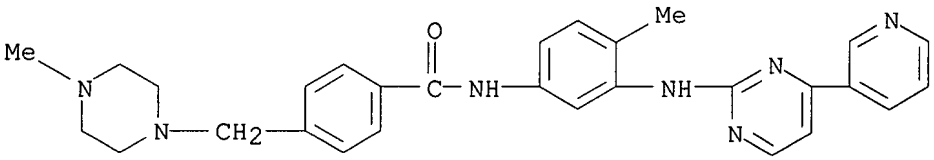
CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 56 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:750535 CAPLUS
DN 141:325332
TI TP53 codon 72 polymorphism in patients with chronic myeloid leukemia
AU Bergamaschi, Gaetano; Merante, Serena; Orlandi, Ester; Galli, Anna; Bernasconi, Paolo; Cazzola, Mario
CS Department of Internal Medicine, University of Pavia Medical School and IRCCS Policlinico San Matteo, Pavia, 27100, Italy
SO Haematologica (2004), 89(7), 868-869
CODEN: HAEMAX; ISSN: 0390-6078
PB Ferrata Storti Foundation
DT Journal
LA English
AB A single nucleotide polymorphism at TP53 codon 72 means that 2 alleles exist: A1 (Pro residue, Pro72) and A2 (Arg residue, Arg72). The Pro72 variant of p53 has a lower apoptotic potential. We found that allele A1 was more frequent in patients with chronic myeloid leukemia (CML) than in controls, and among CML patients who had no cytogenetic response than among responders.
IT 152459-95-5, Imatinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(TP53 codon 72 polymorphism in chronic myeloid leukemia related to imatinib resistance)
RN 152459-95-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)

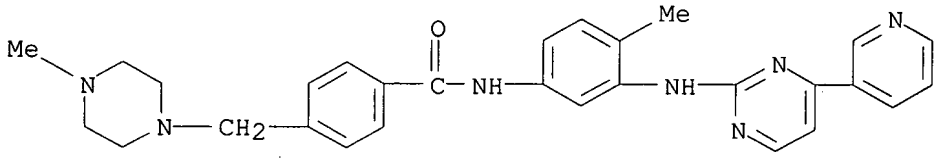


RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 57 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:471551 CAPLUS
DN 142:16188
TI CYP3A5 genotype and midazolam clearance in Australian patients receiving chemotherapy
AU Wong, Mark; Balleine, Rosemary L.; Collins, Michael; Liddle, Christopher; Clarke, Christine L.; Gurney, Howard
CS Westmead Institute for Cancer Research, New South Wales, Australia
SO Clinical Pharmacology & Therapeutics (St. Louis, MO, United States) (2004), 75(6), 529-538
CODEN: CLPTAT; ISSN: 0009-9236
PB Elsevier Inc.
DT Journal
LA English
AB Objectives: Cytochrome P 450 (CYP) 3A enzymes are key metabolizing enzymes for many chemotherapeutic agents, and detection of functionally significant CYP3A genetic variants may be useful in predicting interpatient variation of drug clearance. We have examined the significance of CYP3A5*3 single-nucleotide polymorphism to overall CYP3A activity in vivo in a predominantly Caucasian Australian cancer population. Methods: Screening for wild-type CYP3A5*1 and CYP3A5*3 single nucleotide polymorphism by use of Taqman MGB probe allelic discrimination was performed in 67 patients with cancer (58 Caucasian patients). CYP3A activity was documented via clearance of either oral or i.v. midazolam in 64 patients. Results: All patients had at least 1 CYP3A5*3 allele, and 9 (13%) patients were heterozygous for CYP3A5*3 and CYP3A5*1. Within the subset of Caucasian patients, 6 of 58 (10%) were CYP3A5*1/*3 heterozygotes. Mean midazolam clearance was 1.7 times higher in CYP3A5*1/*3 subjects than in CYP3A5*3/*3 subjects (95% confidence interval, 1.15-2.51; P =.01, 2-way ANOVA). Conclusion: Overall CYP3A activity is related to CYP3A5 genotype. CYP3A5 genotyping may be helpful in predicting the drug-metabolizing capability of individual cancer patients who are predominantly Caucasian in origin.
IT 220127-57-1, Imatinib mesylate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CYP3A5*3 SNP affects overall CYP3A activity evident from higher midazolam clearance in CYP3A5*1/*3 Australian cancer patient receiving chemotherapy and CYP3A5 genotyping may help predict drug-metabolizing ability of Caucasian cancer patient)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

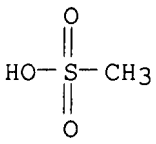
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S

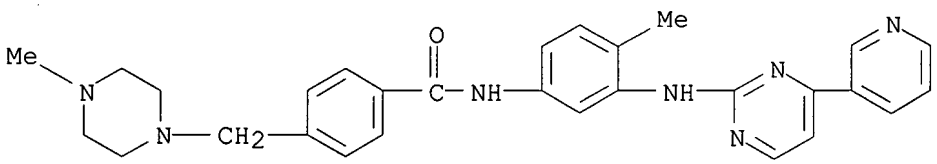


RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 58 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:355114 CAPLUS
DN 140:368656
TI Genetic polymorphisms and gene expression profiles to predict edema as a side effect of tyrosine kinase inhibitor drug treatment
IN Dressman, Marlene Michelle; Kudaravalli, Sridhar; Malinowski, Rachel Helene; McLean, Lee Anne; Polymeropoulos, Mihael Hristos
PA Novartis A.-G, Switz.; Novartis Pharma G.m.b.H.
SO PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004035822	A1	20040429	WO 2003-EP11377	20031014
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SE, SG, SK, SY, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW				
	RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
	CA 2501095	A1	20040429	CA 2003-2501095	20031014
	AU 2003271725	A1	20040504	AU 2003-271725	20031014
	EP 1554400	A1	20050720	EP 2003-753554	20031014
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	BR 2003015344	A	20050823	BR 2003-15344	20031014
	CN 1711361	A	20051221	CN 2003-80103485	20031014
	JP 2006502722	T	20060126	JP 2004-544224	20031014
	US 2006188878	A1	20060824	US 2006-530391	20060202
PRAI	US 2002-418556P	P	20021015		
	WO 2003-EP11377	W	20031014		

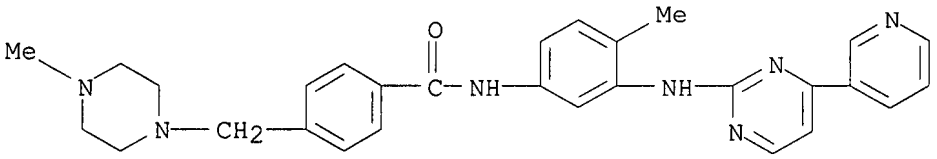
AB This invention provides methods to predict the likelihood of occurrence of the side effect of edema in patients treated with a drug including, but not limited to, a TKI, such as Imatinib or GLEEVEC/GLIVEC. The methods employed use gene expression profile comparisons and the determination of specific SNPs and in the IL-1β gene. Methods of treatment of edema and kits for the performance of the above assays are also provided.
IT 152459-95-5, Imatinib 220127-57-1, GLEEVEC
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(TKI drug therapy; genetic polymorphisms and gene expression profiles to predict edema as side effect of tyrosine kinase inhibitor drug treatment)
RN 152459-95-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME).

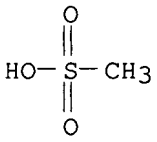
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



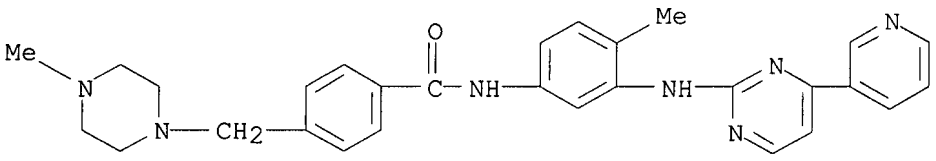
CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 59 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:290903 CAPLUS
DN 141:360256
TI Correlation of major cytogenetic response with a pharmacogenetic marker in chronic myeloid leukemia patients treated with imatinib (STI571)
AU Dressman, Marlene A.; Malinowski, Rachel; McLean, Lee Anne; Gathmann, Insa; Capdeville, Renaud; Hensley, Martee; Polymeropoulos, Mihael H.
CS Clinical Pharmacogenetics, Novartis Pharmaceuticals Corp., Gaithersburg, MD, USA
SO Clinical Cancer Research (2004), 10(7), 2265-2271
CODEN: CCREF4; ISSN: 1078-0432
PB American Association for Cancer Research
DT Journal
LA English
AB Imatinib, an inhibitor of the Bcr-Abl tyrosine kinase, is indicated for the treatment of patients with Philadelphia chromosome-pos. chronic myeloid leukemia. We examined genotypes from patients enrolled in the International Randomized Study of IFN-α vs. STI571 to identify factors that associate with cytogenetic response. Sixty-eight polymorphic loci in 26 genes were examined in a subset of 187 patients (imatinib-treated patients, n = 113; IFN + 1-β-D-arabinofuranosylcytosine-treated patients, n = 74). Correlations between genotype and major cytogenetic response (MCyR) were examined by Fisher's exact tests. Multivariate and survival analyses were also performed. A significant association between MCyR and the rs2290573 polymorphism mapped to 15q22.33 was observed in imatinib-treated patients (P = 0.00037, Bonferroni corrected P = 0.025). Individuals with a CC genotype at this locus had a MCyR rate of 52% compared with individuals with a CT or TT genotype that had a MCyR rate of 89% (odds ratio, 6.72; 95% confidence interval, 1.51-29.91). In a multivariate anal., the rs2290573 polymorphism was significant, whereas Sokal score was not. Time to progression anal. illustrated a significant difference based on genotype for the rs2290573 polymorphism. A significant association was identified between the genetic polymorphism rs2290573 and MCyR in imatinib-treated patients. This polymorphism is located in the intronic sequence of a putative gene with a tyrosine kinase domain. Multivariate anal. suggests that an individual's genotype for rs2290573 has more predictive value for MCyR than prognostic variables such as Sokal score. The clin. relevance of these results requires validation in future clin. trials.
IT 152459-95-5, Imatinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(major cytogenetic response was associated with genetic polymorphism rs2290573 of pharmacogenetic marker putative tyrosine kinase gene DKFZP434C131 in CML patients treated with BCR-ABL tyrosine kinase inhibitor imatinib)
RN 152459-95-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)

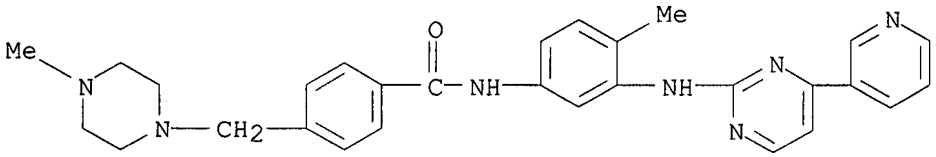


RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD

L17 ANSWER 60 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:279313 CAPLUS
DN 141:150551
TI Preexistence and evolution of imatinib mesylate-resistant clones in chronic myelogenous leukemia detected by a PNA-based PCR clamping technique. [Erratum to document cited in CA140:022690]
AU Kreuzer, K.-A.; le Coutre, P.; Landt, O.; Na, I.-K.; Schwarz, M.; Schultheis, K.; Hochhaus, A.; Doerken, B.
CS Medizinische Klinik m.S. Haematologie und Onkologie, Universitaetsklinikum Charite, Humboldt-Universitaet zu Berlin, Berlin, 13353, Germany
SO Annals of Hematology (2003), 82(10), 660
CODEN: ANHEE8; ISSN: 0939-5555
PB Springer-Verlag
DT Journal
LA English
AB The first three authors (K.-A. Kreuzer, P. le Coutre, and O. Landt) contributed equally to this work and should all be seen equally as its "first author".
IT 220127-57-1, Imatinib mesylate
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preexistence and evolution of imatinib mesylate-resistant clones in chronic myelogenous leukemia detected by PNA-based PCR clamping technique (Erratum))
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

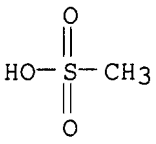
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



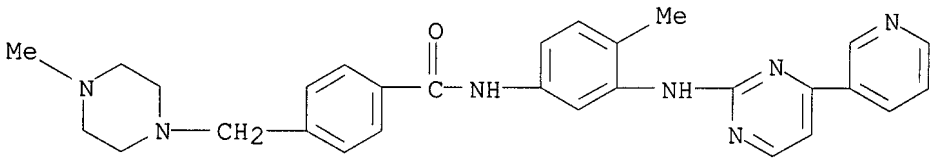
L17 ANSWER 61 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:837315 CAPLUS
DN 139:333140
TI Single nucleotide polymorphisms and expression markers to predict patient responsiveness to tyrosine kinase inhibitors in treatment of Philadelphia chromosome-related neoplasms
IN Dressman, Marlene Michelle; McLean, Lee Anne; Polymeropoulos, Mihael Hristos
PA Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SO PCT Int. Appl., 136 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003087404	A1	20031023	WO 2003-EP4007	20030416
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SE, SG, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW				
	RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
	AU 2003227639	A1	20031027	AU 2003-227639	20030416
	EP 1497463	A1	20050119	EP 2003-725048	20030416
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	JP 2005522221	T	20050728	JP 2003-584342	20030416
	US 2005164196	A1	20050728	US 2003-510969	20030416
PRAI	US 2002-373206P	P	20020417		
	US 2002-431583P	P	20021206		
	WO 2003-EP4007	W	20030416		

AB This invention relates to the use of two form of genomic anal. to predict responsiveness of patients with tyrosine kinase responsive such as Philadelphia chromosome pos. leukemia to treatment with tyrosine kinase inhibitor drugs. Specifically, a set of 55 genes showing altered expression in Philadelphia chromosome-pos. cells is described for use in gene expression profiling of drug responses and a set of set of single nucleotide polymorphisms that show a correlation with a therapeutic response to imatinib mesylate are identified.
IT 220127-57-1, Imatinib mesylate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(SNPs and expression markers to predict patient responsiveness to tyrosine kinase inhibitors in treatment of Philadelphia chromosome-related neoplasms)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

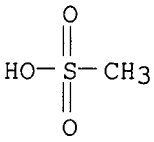
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S

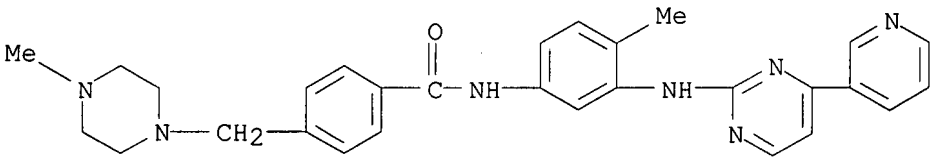


RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 62 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:763179 CAPLUS
DN 140:26188
TI Uterine sarcomas express KIT protein but lack mutation(s) in exon 11 or 17 of c-KIT
AU Rushing, R. Scott; Shajahan, Shahin; Chendil, Damodaran; Wilder, James L.; Pulliam, Joseph; Lee, Eun Y.; Ueland, Frederick R.; van Nagell, John R.; Ahmed, Mansoor M.; Lele, Subodh M.
CS Division of Gynecologic Oncology, University of Kentucky College of Medicine, Lexington, KY, 40536, USA
SO Gynecologic Oncology (2003), 91(1), 9-14
CODEN: GYNOA3; ISSN: 0090-8258
PB Elsevier Science
DT Journal
LA English
AB Several tumors express the protein product of the protooncogene c-KIT. Some of these respond to imatinib mesylate, a tyrosine kinase inhibitor. The tumors that respond frequently have mutation(s) in exon 11 of c-KIT that encodes for the regulatory juxtamembrane helix. Some tumors that express KIT protein have mutation(s) in exon 17 of c-KIT; however, these do not respond to imatinib mesylate. This investigation was performed to determine the expression of KIT protein and mutational status of exons 11 and 17 of c-KIT in uterine sarcomas. Twenty-five uterine sarcomas treated from 1990 to 2002 were evaluated. These included 14 malignant mullerian mixed tumors (MMMT), 7 leiomyosarcomas (LMS), 2 endometrial stromal sarcomas (ESS), and 2 high-grade heterologous sarcomas (HGHS). Formalin-fixed, paraffin-embedded tissue sections were immunostained with anti-KIT antibody (Santa Cruz Biotechnol., Santa Cruz, CA) with a semiquant. assessment. Normal myometrium when present in the section was used as an internal neg. control. Areas of tumor were microdissected followed by DNA extraction, polymerase chain reaction (PCR) amplification of exons 11 and 17, single-strand conformational polymorphism (SSCP), and DNA sequencing to detect the presence of mutation(s). All 25 tumors expressed KIT protein at varying levels as assessed by immunohistochem. The staining was diffuse and of moderate to strong intensity in 22 tumors. In three tumors (one of each type except MMMT) the staining intensity was weak. In MMMT the epithelial and sarcomatous foci stained similarly. No mutation(s) in exons 11 or 17 of c-KIT were identified in 24/25 tumors. One LMS had deletion of both exons 11 and 17. Although uterine sarcomas express KIT protein, they lack KIT-activating mutation(s) in exon 11 or 17 of c-KIT. Therefore, these tumors are unlikely to respond to imatinib mesylate.
IT 220127-57-1, Imatinib mesylate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(KIT protein of uterine sarcomas lacking mutation(s) in exon 11 or 17 of gene c-KIT and antitumor agent response thereof)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

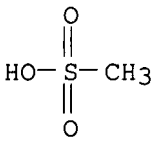
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



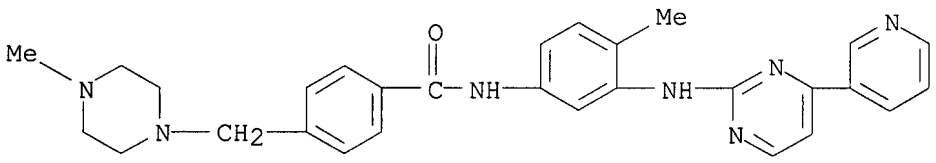
CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 63 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:575172 CAPLUS
DN 139:390897
TI Presence of the BCR-ABL mutation Glu255Lys prior to STI571 (imatinib) treatment in patients with Ph+ acute lymphoblastic leukemia
AU Hofmann, Wolf-Karsten; Komor, Martina; Wassmann, Barbara; Jones, Letetia C.; Gschaidmeier, Harald; Hoelzer, Dieter; Koeffler, H. Phillip; Ottmann, Oliver G.
CS Department of Hematology, University Hospital, Frankfurt/Main, Germany
SO Blood (2003), 102(2), 659-661
CODEN: BLOOAW; ISSN: 0006-4971
PB American Society of Hematology
DT Journal
LA English
AB The tyrosine kinase inhibitor STI571 (imatinib) binds competitively to the ATP (ATP) binding site of the ABL kinase, thereby inhibiting auto- and substrate phosphorylation of the oncogenic protein BCR-ABL and preventing the activation of downstream signaling pathways. Comparative studies on leukemic cell samples obtained from chronic myelogenous leukemia (CML) and Philadelphia chromosome-pos. (Ph+) acute lymphoblastic leukemia (ALL) patients before and after treatment with STI571 reported point mutations in resistant samples after a short time of therapy. The aim of this study was to determine whether patients with Ph+ ALL in whom resistance developed as a consequence of the Glu255Lys mutation already harbored this subclone prior to STI571 treatment. First, the migration pattern of cDNAs from 30 bone marrow samples from patients with Ph+ ALL was analyzed by polymerase chain reaction-single strand conformation polymorphism (PCR-SSCP). Thereafter, detailed mutational anal. using genomic DNA was performed on initial STI571-naive bone marrow samples of 4 individuals with Ph+ ALL, for whom the mutation Glu255Lys in association with STI571 treatment had been shown. A 166-bp PCR fragment spanning from nucleotide (nt) 862 to nt 1027 was cloned, and 108 clones per sample were analyzed by direct sequencing. This more sensitive technique revealed the presence of the Glu255Lys mutation in 2 initial samples, one clone each. We identified for the first time the mutation Glu255Lys in STI571-naive leukemic samples of Ph+ ALL patients. The findings suggest that the mutation exists in a very small subpopulation of leukemic cells at the beginning of STI571 therapy.
IT 152459-95-5, Imatinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(presence of BCR-ABL mutation Glu255Lys prior to STI571 treatment in patients with Ph+ ALL)
RN 152459-95-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)

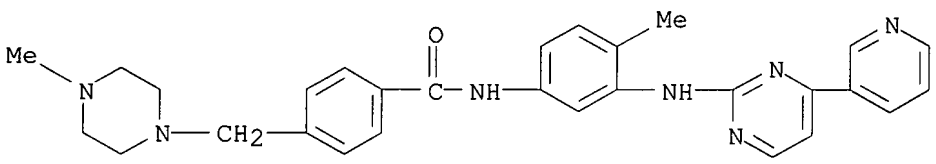


RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 64 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:519030 CAPLUS
DN 140:36491
TI Sensitive and quantitative detection of mutations associated with clinical resistance to STI-571
AU Liu, Wei-Hua; Makrigiorgos, G. Mike
CS Dana Farber Cancer Institute, Department of Radiation Oncology, Harvard Medical School, Boston, MA, 02115, USA
SO Leukemia Research (2003), 27(11), 979-982
CODEN: LEREDD; ISSN: 0145-2126
PB Elsevier Science Ltd.
DT Journal
LA English
AB Resistance to chronic myeloid leukemia (CML) drug STI571 has been associated with point mutations in the kinase domain of BCR-ABL. For example, the mutation T315I (g. 68721C>T) and, to a lesser extent, Y253F (g. 58796A>T) appear in a significant proportion of patients resistant to treatment. Mutations appear intimately related to the development of resistance, and they may pre-exist in a small percentage (<1%) of tumor cells at the time of treatment initiation. Most mutation detection methods, including sequencing, are unable to detect such a small percentage of mutations in a background of wild type sequences. We describe the simplification and modification of a recently developed enhanced PCR-RFLP method, and its application to the detection of T315I and Y253F mutations. The method is quant., can be used in agarose gel or real time PCR formats, and reliably detects 1 mutation-containing cell in a background of almost 1000 non-mutated cells. The increased sensitivity offered by this assay will allow detection of these mutations at an early stage during treatment and will be useful in rational treatment modification and in studies which address the association between these mutations and drug resistance.
IT 220127-57-1, STI 571
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(resistance to; simplified enhanced PCR-RFLP method for detection of two common mutations (T315I and Y253F) in human BCR-ABL gene associated with clin. resistance to STI571)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

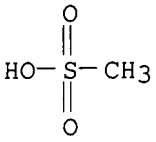
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S

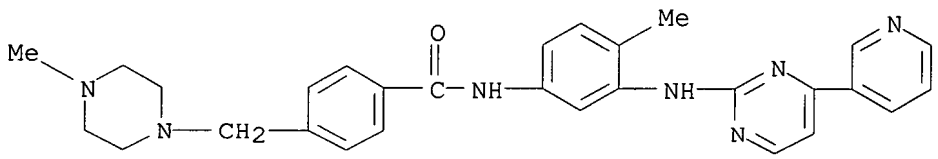


RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 65 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:377376 CAPLUS
DN 139:83024
TI c-kit gene mutation at exon 17 or 13 is very rare in sporadic gastrointestinal stromal tumors
AU Kinoshita, Kazuo; Isozaki, Koji; Hirota, Seiichi; Nishida, Toshirou; Chen, Hui; Nakahara, Masanori; Nagasawa, Yutaka; Ohashi, Akiko; Shinomura, Yasuhisa; Kitamura, Yukihiko; Matsuzawa, Yuji
CS Department of Internal Medicine and Molecular Science, Graduate School of Medicine, Osaka University Medical School, Suita, 565-0871, Japan
SO Journal of Gastroenterology and Hepatology (2003), 18(2), 147-151
CODEN: JGHEEO; ISSN: 0815-9319
PB Blackwell Publishing Asia Pty Ltd.
DT Journal
LA English
AB Gastrointestinal stromal tumors (GIST) are the most common mesenchymal tumors of the human gut. They frequently have gain-of-function mutations of the c-kit gene, which encodes a receptor, tyrosine kinase. The mutations were found at exon 11 in most cases, and either at exon 9 or at exon 13 in rare cases. Recently, we found a family with multiple GIST and a gain-of-function mutation at exon 17. The family was the first reported GIST case with c-kit gene mutation at exon 17 including sporadic GIST. Although we previously reported that the c-kit gene mutation at exon 17 was not detected in 124 sporadic GIST by single-strand conformation polymorphism (SSCP) anal., the mutation at exon 17 observed in the familial GIST was detectable by the use of direct sequencing but not by our SSCP method. In the present study, we examined the mutations at exon 17 and exon 13 by using direct sequencing. Genomic DNA was extracted from formalin-fixed, paraffin-embedded GIST tissues. We could obtain 143 sporadic GIST cases appropriate for DNA anal. at exon 17 and 141 at exon 13. Exons 17 and 13 were amplified by using polymerase chain reaction and direct sequencing was conducted. No mutation was found at exon 17, and only one case with the mutation at exon 13 was observed The GIST with the mutation at exon 13 was large and showed frequent mitosis, and the patient died of the recurrent GIST 3 yr after the first operation. The mutation at exons 17 or 13 was considered to be very rare in sporadic GIST.
IT 220127-57-1, STI571
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of tyrosine kinase inhibitor STI571 on c-kit gene mutation at exon 17 or 13 in human sporadic gastrointestinal stromal tumors)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

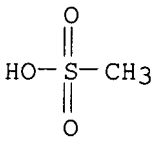
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S

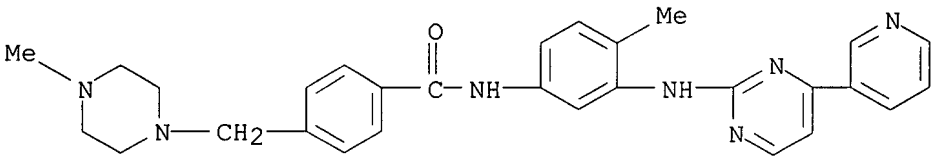


RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 66 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:362915 CAPLUS
DN 139:78858
TI Imatinib therapy for hypereosinophilic syndrome and other eosinophilic disorders
AU Pardanani, Animesh; Reeder, Terra; Porrata, Luis F.; Li, Chin-Yang; Tazelaar, Henry D.; Baxter, E. Joanna; Witzig, Thomas E.; Cross, Nicholas C. P.; Tefferi, Ayalew
CS Divisions of Hematology and Internal Medicine, Hematopathology, and Laboratory Medicine and Pathology, Mayo Clinic, Rochester, MN, 55905, USA
SO Blood (2003), 101(9), 3391-3397
CODEN: BLOOAW; ISSN: 0006-4971
PB American Society of Hematology
DT Journal
LA English
AB Imatinib mesylate (Gleevec), a small mol. inhibitor of abl, kit, and platelet-derived growth factor receptor (PDGFR) tyrosine kinases, has been reported to be effective in the treatment of hypereosinophilic syndrome (HES) and a rare eosinophilia-associated chronic myeloid disorder (eos-CMD) characterized by the t(5;12)(q33;p13) cytogenetic abnormality. In the current study, we sought to confirm the preliminary observations in HES as well as evaluate the therapeutic value of imatinib in eos-CMD that is not associated with t(5;12)(q33;p13). Five patients with HES (all men, median age = 46 yr) and 2 with eos-CMD (both men, aged 45 and 58 yr) were treated with imatinib at a starting dose of 100 to 400 mg/day. Cytogenetic studies showed no evidence of either the bcr-abl translocation or t(5;12)(q33;p13) in any patient. Screening of exons encoding the intracellular catalytic domains and extra-cellular ligand binding domains of PDGFRβ (exons 2-23) and c-kit (exons 1-21) in 6 patients demonstrated mostly previously known polymorphisms. At a median follow-up of 17 wk (range, 10-33 wk), 2 patients with HES and 1 with eos-CMD have achieved complete clin. remission and 1 addnl. patient with HES has achieved a partial remission. In contrast to previous observations, all 4 responding patients had elevated serum interleukin-5 levels. Although the drug was well tolerated in most patients, a previously unrecognized treatment toxicity of acute left ventricular dysfunction occurred in a responding patient with HES within the first week of treatment. Myocardial biopsy revealed eosinophilic infiltration and degranulation, and the cardiogenic shock was reversed with the prompt institution of corticosteroid therapy.
IT 220127-57-1, Gleevec
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(imatinib mesylate (Gleevec) for hypereosinophilic syndrome and other eosinophilic disorders)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

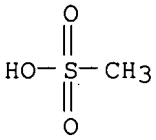
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S

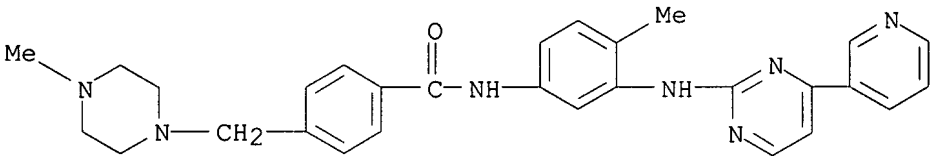


RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 67 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:353042 CAPLUS
DN 140:22690
TI Preexistence and evolution of imatinib mesylate-resistant clones in chronic myelogenous leukemia detected by a PNA-based PCR clamping technique
AU Kreuzer, K.-A.; le Coutre, P.; Landt, O.; Na, I.-K.; Schwarz, M.; Schultheis, K.; Hochhaus, A.; Doerken, B.
CS Medizinische Klinik m.S. Haematologie und Onkologie, Universitaetsklinikum Charite, Humboldt-Universitaet zu Berlin, Berlin, 13353, Germany
SO Annals of Hematology (2003), 82(5), 284-289
CODEN: ANHEE8; ISSN: 0939-5555
PB Springer-Verlag
DT Journal
LA English
AB Recently, various mutations within the Abl sequence have been described that neg. affect imatinib binding to Bcr/Abl resulting in cellular resistance of chronic myeloid leukemia (CML) cells. So far, little is known as to whether these mutations are preexisting or develop under imatinib therapy as current mutation analyses are limited by a low sensitivity of approx. 1:2 (50%) to 1:5 (20%). By combining peptide nucleic acid (PNA)-based DNA clamping with a fluorescence hybridization probe assay, we developed a new and highly sensitive technique for the detection of known mutations within the Bcr/Abl kinase domain. With this approach we investigated 19 cases of CML refractory to imatinib treatment before and during therapy. By clamping of wild-type Abl through PNA we could effectively enhance the detection sensitivity for the Bcr/Abl mutations Thr315Ile, Glu255Lys, and Tyr253His such that 1 mutant cDNA mol. could be detected in 500 negatives (0.2%). We observed in one case that a Gly255Lys mutation was detectable before treatment. By DNA anal. of buccal swaps, a genetic polymorphism could be excluded. In two cases clonal evolution of known mutations developed gradually under treatment. In another case an initially detectable Tyr253His mutation disappeared after therapy onset but was again observed after 6 wk of imatinib treatment. Preexisting and evolving Bcr/Abl mutations associated with an unfavorable prognosis could be safely detected by the presented technique. This may facilitate risk stratification in CML and may serve as a model for individualized mol. monitoring and therapeutic strategies in other malignant diseases.
IT 220127-57-1, Imatinib mesylate
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preexistence and evolution of imatinib mesylate-resistant clones in chronic myelogenous leukemia detected by PNA-based PCR clamping technique)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

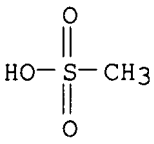
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S

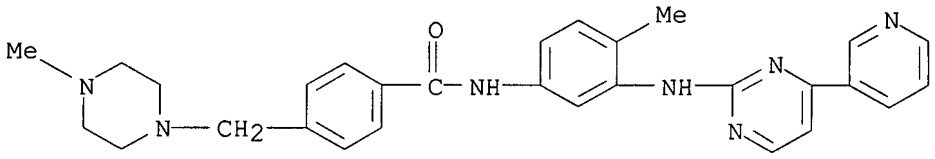


RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 68 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:206383 CAPLUS
DN 139:94948
TI Lack of c-kit exon 11 activating mutations in c-KIT/CD117-positive SCLC tumour specimens
AU Burger, H.; den Bakker, M. A.; Stoter, G.; Verweij, J.; Nooter, K.
CS Department of Medical Oncology, Erasmus MC, Rotterdam, 3000 DR, Neth.
SO European Journal of Cancer (2003), 39(6), 793-799
CODEN: EJCAEL; ISSN: 0959-8049
PB Elsevier Science Ltd.
DT Journal
LA English
AB Previous studies have shown that STI571, a selective tyrosine kinase inhibitor of c-KIT, is highly effective in c-KIT/CD117-pos. gastrointestinal stromal tumors (GIST), especially those that have activating mutations in the c-kit exon 11 that encodes the juxtamembrane (JM) domain of the c-KIT oncoprotein. We examined the prevalence of activating exon 11 c-kit mutations in 26 small-cell lung cancer (SCLC) cases to explore whether this disease is also a potential target for treatment with STI571. Expression of c-KIT, estimated by immunohistochem., was demonstrated in 14 out of 22 SCLC samples (64%); 9 samples showed moderate to strong staining (41%), 5 samples were weakly pos. (23%), whereas 8 samples (36%) were neg. for CD117. Next, the authors examined the mutational status of exon 11 of the c-kit gene, by single-stranded conformational polymorphism (SSCP) and sequencing in all of the cKIT/CD117-pos. tumors. However, no activating mutations in the c-kit exon 11 were found by either technique. Apparently, c-KIT oncoprotein expression in SCLC was not correlated with activating mutations in c-kit exon 11. In analogy to GISTs,these results could imply that SCLC patients would not benefit from treatment with STI571.
IT 220127-57-1, STI571
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(STI571 without therapeutic effect on small cell lung cancer due to lack of c-kit exon 11 activating mutations)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

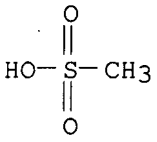
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



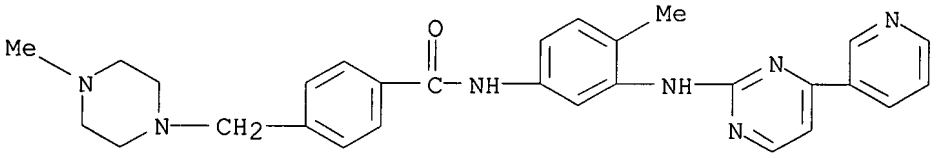
CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 69 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:11148 CAPLUS
DN 139:78604
TI Telomere length in peripheral blood granulocytes reflects response to treatment with imatinib in patients with chronic myeloid leukemia
AU Brummendorf, Tim H.; Ersoz, Inci; Hartmann, Ulrike; Bartolovic, Kerol; Balabanov, Stefan; Wahl, Alexandra; Paschka, Peter; Kreil, Sebastian; Lahaye, Tanja; Berger, Ute; Gschaidmeier, Harald; Bokemeyer, Carsten; Hehimann, Rudiger; Dietz, Klaus; Lansdorp, Peter M.; Kanz, Lothar; Hochhaus, Andreas
CS Department of Hematology and Oncology, University Medical Center II, Tubingen, 72076, Germany
SO Blood (2003), 101(1), 375-376
CODEN: BLOOAW; ISSN: 0006-4971
PB American Society of Hematology
DT Journal
LA English
AB Age-adjusted telomere length in peripheral blood (PB) granulocytes was correlated with response to treatment with imatinib in chronic myeloid leukemia patients. An association between the duration of imatinib treatment and telomere length in the PB was observed Telomere length in these patients varied depending on the degree of cytogenetic and mol. responses achieved during imatinib therapy. The results reflect a steadily increasing fraction of Philadelphia chromosome-neg. cells (with normal or only slightly reduced telomere length) contributing to the PB cell pool in patients receiving imatinib treatment.
IT 152459-95-5, Imatinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(telomere length in peripheral blood granulocytes reflects response to treatment with imatinib in patients with chronic myeloid leukemia in relation to Philadelphia chromosome)
RN 152459-95-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 70 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2002:813883 CAPLUS
DN 137:304767
TI Akt and regulation of rheumatoid arthritis synovial fibroblast apoptosis
IN Mountz, John D.; Zhang, Huang-Ge; Xie, Jin-Fu; Liang, Xu; Yang, Pingar; Hsu, Hui-Chen
PA UAB Research Foundation, USA
SO PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002083075	A2	20021024	WO 2002-US11820	20020416
WO 2002083075	A3	20040304		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2444840	A1	20021024	CA 2002-2444840	20020416
AU 2002303354	A1	20021028	AU 2002-303354	20020416
EP 1414500	A2	20040506	EP 2002-731374	20020416
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRAI US 2001-283966P	P	20010416		
WO 2002-US11820	W	20020416		

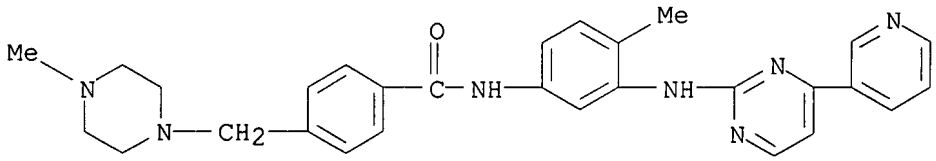
AB The administration of an Akt inhibitor in a suitable carrier to a rheumatoid arthritis synovial fibroblast affords a process for inducing rheumatoid arthritis synovial fibroblast apoptosis. The Akt inhibitor is administered either as an active mol. or as a gene sequence expressible within rheumatoid arthritis synovial fibroblast cells. The gene sequence can be encompassed within a gene vector such as an adenovirus. A process for assaying rheumatoid arthritis drug candidates for apoptosis affect includes exposing a culture of rheumatoid arthritis synovial fibroblast cells to a drug candidate and monitoring apoptosis in the culture in the presence of the drug candidate. Apoptosis in the culture is compared to apoptosis induced in a duplicate culture in the presence of a known Akt inhibitor.

IT 220127-57-1, CGP57148B
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Akt and regulation of rheumatoid arthritis synovial fibroblast apoptosis)

RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

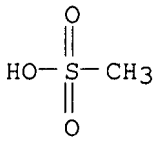
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

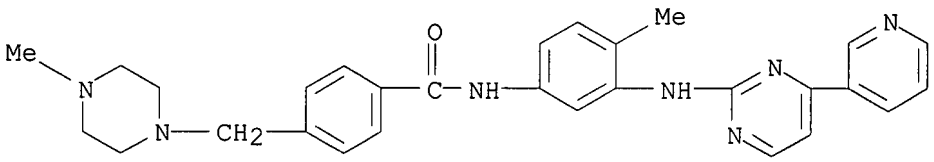
CRN 75-75-2
CMF C H4 O3 S



L17 ANSWER 71 OF 71 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2002:584678 CAPLUS
DN 138:180305
TI Several types of mutations of the abl gene can be found in chronic myeloid leukemia patients resistant to STI571, and they can pre-exist to the onset of treatment
AU Roche-Lestienne, Catherine; Soenen-Cornu, Valerie; Grardel-Duflos, Nathalie; Lai, Jean-Luc; Philippe, Nathalie; Facon, Thierry; Fenaux, Pierre; Preudhomme, Claude
CS Unite Inserm U524, Lille, 59045, Fr.
SO Blood (2002), 100(3), 1014-1018
CODEN: BLOOAW; ISSN: 0006-4971
PB American Society of Hematology
DT Journal
LA English
AB Targeting the tyrosine kinase activity of BCR-ABL represents a very promising therapeutic strategy in chronic myeloid leukemia (CML). Despite strong efficacy of the tyrosine kinase inhibitor STI571, resistance has been observed in a significant proportion of patients in advanced CML stage or in Ph-pos. acute lymphoid leukemia (ALL). We investigated in this study the mechanism of resistance to STI571 through point mutations in the tyrosine kinase domain and/or BCR-ABL gene amplification in 24 patients (16 in chronic phase and 8 in accelerated phase of the disease) who obtained no cytogenetic response to STI571 treatment. Screening for the already-described Thr315Ile point mutation in the ABL domain using a reverse transcription polymerase chain reaction restriction fragment length polymorphism (RT-PCR-RFLP) technique, 3 patients showed a proportion of mutated transcript at the time of resistance. The same technique failed to detect mutation at diagnosis, but a specific allele-specific oligonucleotide (ASO)-PCR on DNA for the Thr315Ile mutation and, after sequencing, for 2 newly described Phe311Leu and Met351 Thr substitutions, showed the presence of rare mutated cells prior to STI571 therapy. Furthermore, the increased proportion of mutated cells during treatment detected by ASO-PCR strongly suggested clonal selection by the functional inhibiting effect of these mutations. Finally, no BCR-ABL gene amplification was detected by fluorescent in situ hybridization (FISH) in the 24 STI571-resistant patients. Our data support that in CML patients treated with STI571, ABL mutations are not restricted to the accelerated phase of the disease and that, at least in some cases, mutations seem to occur prior to STI571 therapy, probably as second mutational events during the course of CML.
IT 220127-57-1, STI571
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mutation types of abl gene found in TK inhibitor STI571-resistant chronic myeloid leukemia patients)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

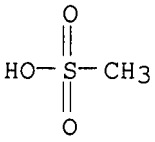
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
=> log y
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                      ENTRY    SESSION
FULL ESTIMATED COST                                   417.12     599.33

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                      ENTRY    SESSION
CA SUBSCRIBER PRICE                                   -60.06     -60.06

STN INTERNATIONAL LOGOFF AT 17:23:27 ON 21 SEP 2007
```